BUREAU OF HYGIENE AND TROPICAL DISEASES

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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

OFFICE. **Report on the Health of the Army 1956. Section 2.—Statistical Section.** pp. iv + 89, 3 figs. 960, Feb. London. [W.O. Code No. 12715 (Section 2); 24/General/4072.]

the introduction to Section 2—the Statistical Section ie Report on the Health of the Army 1956—it is l that the publication of Medical Documentation, (W.O. Code No. 11381) "was an important step rds improving the quality of the data on which of the fabric of the Army's medical statistics must sed".

e first 4 parts of the report contain detailed tables lescription of total hospital admissions, medical-non-ives and morbidity rates and trends in the different nands. Morbidity rates are given per 1,000 strength isease groups and individual diseases. "The only se groups which produce an admission rate of more 1% of strength everywhere are, first, tonsillitis and ngitis and, secondly, skin conditions." Infections the most common skin disorders and had the highest al rate in Bermuda and the Caribbean area. Venereal se rates varied greatly in the different commands ranged from 1·9 in Malta and 2·3 in the United dom to 238·8 in Korea and Japan. The admission for psychiatric conditions was between 3·5 and 7 ,000 in all commands except in the small commands est Africa (8·6) and Bermuda (9·2).

asonal fluctuations in the admissions for certain dis- in different commands are recorded in tables which the monthly percentages of the annual rates in 1956 pared with the average of 1949–1955.

ich detailed information is given on medical dis- es from the army (the highest rate being for psychia- lisorders), deaths in the army by disease and injury reatment provided by the Army Dental Service.

her parts of the report give (1) measurements of nts and heights of regulars and national servicemen ear of birth and (2) detailed tables of rates of admis- to medical units in different commands for stated diseases of men of 7 age-groups (from under 19 to over 45 years) to illustrate age trends in morbidity.

Special enquiries and investigations undertaken were:—(1) the possibility of a seasonal change in weight and (2) the association of medical discharges with initial grading. A survey of soldiers from Glasgow was made and some of the relevant data are presented here and contrasted with those from the Army as a whole. Tables give information on medical grading at various times, admissions to medical units, discharges from the Army for medical reasons, military rank on release and average height and weight on entry and release.

In Part XIV of the report there are short descriptions of special investigations on appendicitis, deaths due to electrocution, frostbite, locomotor and visual defects and thyrotoxicosis.

The last part consists of tables of hospital admissions and invalidings by annual rates per 1,000 strength in each year in the periods 1901–1914, 1921–1938 and 1946–1956. Admission rates for enteric fever comparing 1901 and 1956 were reduced from 5·9 to 0·0, for malaria from 119·1 to 0·6, for venereal disease from 133·7 to 11·4 and for tuberculosis from 4·4 to 0·9. The invaliding rate for tuberculosis in 1901 was 1·8 and 1·1 in 1956 but for psychiatric conditions increased from 1·4 to 5·1. [For the 1955 Report, see this *Bulletin*, 1960, v. 35, 3.]

M. E. Delafield

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 194. **Local Health Service. Third Report of the Expert Committee on Public Health Administration. Geneva, 12–17 October 1959.** 49 pp. [Refs. in footnotes.] 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

The committee contained 7 members including one British delegate, Sir Andrew DAVIDSON. The chairman was

Dr. G. ARBONA of Puerto Rico. The secretariat also contained 7 members, 2 of them British, Professor J. M. MACKINTOSH and Dr. R. C. HOLDERNESS MOH of Loughborough. The 2 previous reports were published in 1952 and 1954 [this *Bulletin,* 1954, v. 29, 909.]

The body of the report explains why it was decided to arrange for *Pilot Studies on Local Health Service* to be undertaken and the appendices set out the information which it was hoped to obtain from the surveys and summaries of the 6 reports received. The information desired was divided into the community and the family approach and "fell into 3 general categories: (1) general information, including environmental, social and cultural aspects; (2) specific information on such matters as diet and nutrition; and (3) data relating to illness and the use of medical services, including the patient's attitude to ill health".

The reports studied came from (1) Ramanagaram Health Training Area, Mysore, India; (2) Zutphen, Netherlands; (3) Trujillo Alta, Puerto Rico; (4) Kronoberg County, Sweden; (5) an area in the Zulu Reserve, Natal, South Africa; (6) Loughborough, England.

The difficulties in obtaining accurate information about diet and family incomes are discussed and the need to pay quite frequent visits to get particulars about illness is stressed. In most cases the questionnaires were completed by public health nurses or health visitors under medical supervision.

An analysis of such surveys is a valuable means of self-appraisal and a preliminary step towards research.

Further development of the local health services involves expansion of the domiciliary care programme; enlistment of general medical practitioners in preventive work; improvements in health service records; the provision of reference centres, primary and national, to which problems beyond local resources can be referred. The great value of good and comprehensive annual reports from local administrative areas is mentioned.

Allen Daley

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 193. **Teacher Preparation for Health Education. Report of a Joint WHO/UNESCO Expert Committee. Geneva, 2–7 November 1959.** 19 pp. 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office. [1s. 9d.; $0.30; Sw.fr. 1.–.]

"This report deals with the preparation of the great body of elementary and secondary school teachers for their part in the health education aspects of the school programme. The Committee considers that the p sional education of school administrators would pr ably include a similar preparation."

This Technical Report No. 193 in the World H Organization Series is short and clearly written. I 11 sections which contain description, discussion an gestions on (1) the teacher's part in health educati present status of teacher preparation for health educ (3) objectives, (4) what the teacher needs to kno learning experiences in health education during service preparation, (6) in-service education, (7) pla of teacher preparation, (8) leadership in teacher pr tion and (9) future developments, studies and res

In the summary to the Report it is said "In conc the task of preparing a flexible framework of g principles on teacher preparation for health educ the Committee recognizes that while the health of dren and youth is primarily a responsibility of p it is of common concern also to educators and workers". *M. E. Dela*

MACQUEEN, Ian A. G. **Evaluation of a Scher Health Education.** *Med. Officer.* 1960, Ma v. 103, No. 21, 295–8.

The Aberdeen Health Guidance Scheme now fourth year was described in outline in a previous cation in 1958 [this *Bulletin,* 1959, v. 34, 185] a evaluation of its influence on health is now presente

There are reports with numerical tables which in (1) reduction in the number of cases taken into lon care by the Children's Department, (2) reduction of bers in the residential nursery, (3) marked reducti juvenile delinquency, (4) a considerable downward of nervousness and mental instability found in s entrants and (5) a great reduction of the waiting li day nurseries. Among other points reported are (1 tive absence of the national increase of gonorrhoea has been officially reported, (2) lowered incidence infectious diseases pertussis, poliomyelitis and e and (3) home accidents have become much less fre Data are also presented on defects found in schoo dren, attendance at child welfare clinics, diphtheria i nization and the mass radiography campaign.

There is a good discussion in which due attent given to the non-specific factors as well as those are specific to or innate in the health education sc

It is stated in conclusion "The value of the Abe health education scheme in the conditions and ci stances of that city is proved beyond shadow of do *M. E. Dela*

VITAL STATISTICS

, G. La situation de la mortalité infantile en Hongrie. [**Infant Mortality in Hungary**] *Santé Publique*. Bucharest. 1959, v. 2, No. 1, 57–69, 7 figs.

he infant mortality in Hungary has fallen steadily e 1920 when it was 200 per 1,000 live births to 131·4 938 and 63·1 in 1957. The decline was interrupted in 5 when the rate rose to 169·1. The seasonal distribu- of infant mortality has undergone a marked change he last 20 years; in 1938 the rate was at a maximum he summer and in 1957 it was at a minimum. The nt mortality in Hungary is almost twice that of the rage of western European countries and this difference pparent in each age-group except at 1–6 days when Hungarian rate is only about 25% in excess. The chief causes of infant deaths are: diseases peculiar to early infancy, 43%; respiratory diseases, 25%; diseases of the digestive system, 11%; and congenital malformations, 10%. Compared with 1938 the chief falls in infant mortality were those of the digestive system, 74%, and infectious diseases, 66%. The infant mortality in the rural districts which was higher than in the towns has shown the greatest improvement and now the rate is only slightly higher than in urban areas. This trend with density of population is the reverse of that in England and Wales where the rural areas had the lowest rates and still have an infant mortality slightly below that of the urban areas.

Compared with 20 years earlier the antenatal and welfare services in Hungary have been considerably improved. The percentage of births occurring in an institution rose from 21% in 1931 to 69% in 1957.

W. J. Martin

EPIDEMIOLOGY

TSON, G. I. **Epidemiology: a Speciality or a Hobby?** *Postgraduate Med. J.* 1960, May, v. 36, No. 415, 317–21, 6 figs. [14 refs.]

his paper is introduced by a quotation from W. N. KLES—" Let me recommend as a hobby, particularly hose young men entering country practice, this obser- ion of the natural history of epidemic diseases ". The hor, who is clearly an enthusiast in this " hobby ", has tten a short and most interesting article in which he cribed first of all the " tools for the job ". These are patience to take good case histories, to capture the erests of patients, to think over the epidemiological aning of signs and symptoms, and to sort and tabulate findings and write up results, (2) making adequate ords, and (3) continuous training in the yearly more nplex sciences which are essential to epidemiological earch.

Examples which are given of the results of collective demiological enquiries by many doctors include (1) t of the faculty of the College of General Practitioners the prevalence of Bornholm disease in south tern England in 1956, and (2) the published report of a oup of 137 family doctors who found that " mild " acks of measles were particularly common in young ants and that the proportion of mild cases was signifi- ntly higher among breast-fed infants than among the ttle-fed in all groups up to the age of 30 months.

From his own experience there is mention of studies the diphasic pattern of the temperature chart in influza, on the duration of infectivity in measles and on the erial interval " between a patient's illness and that of contacts.

There are suggestions for bringing about an increase the number of family doctors who are interested in nical epidemiological research. *M. E. Delafield*

KINGDON, K. H. **Relative Humidity and Air-Borne Infections.** *Amer. Rev. Respiratory Dis.* 1960, Apr., v. 81, No. 4, 504–12, 8 figs. [11 refs.]

The author considers the effect of relative humidity (RH) on the spread of the 1957 influenza epidemic in the United States.

Droplets produced by sneezing contain salt, and in its effect on their behaviour RH may be divided into 4 ranges: (1) 100–96%, droplets remain large and rapidly fall out; (2) 95–86%, droplets lose sufficient weight by evaporation to remain airborne, but salt concentration does not rise high enough to kill the virus; (3) 85–76%, droplets shrink so much that salt concentration is sufficiently high to kill the virus; (4) <75%, salt crystallizes out so quickly that there is no time for the virus to be killed. The author tentatively suggests that in range (2) the droplets are more infective than in range (4), and after describing the conditions under which an epidemic is recognized attempts to use RH data to explain the delay between the introduction of Asian influenza in June 1957 and the appearance of an epidemic the following October.

The spread of the epidemic can be traced by means of United States Public Health Service data on employee absenteeism in 36 cities. In only 6 of those in which absenteeism rose did the temperature remain high enough for external humidity to be relevant indoors, where people crowd together. In some instances the absenteeism ratio (absenteeism during epidemic divided by the absenteeism during corresponding period in the previous year) and the humidity ratio (number of hours in RH range 2 divided by the number of hours in RH range 3) follow the same general trend. *J. McK. Ellison*

HEALTH OF STUDENTS, NURSES AND HOSPITAL STAFFS

SPARKS, J. P. **Medical Practice in a Public School.** *Postgraduate Med. J.* 1960, May, v. 36, No. 415, 309–16.

"Public School medicine as a specialized branch of medical practice has a history of little more than a century." In this interesting paper the author (Medical Officer of Rugby School) gives an outline of this history from the appointment of a resident medical officer to Marlborough College in 1848, with mention of the scanty records of medical practice before this date. "In the 19th century the *Lancet* campaigned vigorously against the poor living conditions, lamentable sanitation, inadequate diet and dubious medical attention available in the schools." Later, in 1884 the Medical Officers of Schools Association was founded and today has about 250 members.

There is also an account of the medical history of Rugby School and the appointment in 1868 as medical officer of Dr. FARQUHARSON who was succeeded by Dr. Clement DUKES, "one of the great figures of public school medicine".

The functions of the medical officer to a public school are discussed and the medical arrangements at Rugby School are fully described. "Since the inception National Health Service in 1948 the boys have placed on the medical officer's list (under the Wa shire Executive Council), holiday treatment else being obtained on the basis of temporary resi Operations and consultations in the sanatorium a tained privately, most parents being insured under the hospital insurance schemes".

Much of this article is devoted to giving "some p of the clinical material—the boys themselves". are some interesting data on the results of intelli tests, variations in the stage of development at a age and on measurements of height and weight in parison with records of these in years past. Expe of infectious diseases is described. No cases of tuberculosis have been discovered in 2 radiographi veys in the last decade. Over 99% of the school p tion has been protected against poliomyelitis by vaccine. Other medical conditions which are cons include enuresis, migraine, acne, allergic rhinor minor sepsis, fungus infections, surgical cases, of acute appendicitis is the commonest, and torsion testicle. Games injuries are described and among rugger injuries are the most frequent numbering 600 a year. *M. E. Dela*

CANCER

DOLL, R. **Smoking and Lung Cancer. Report to the Sub-Committee for the Study of the Risks of Cancer from Air Pollution and the Consumption of Tobacco.** Reprinted from *Acta Unionis Internat. Contra Cancrum.* 1959, v. 15, No. 6, 1283–96, 4 figs. [Numerous refs.]

Dr. Doll presented this report in June, 1958. In it he summarized the evidence then available of the relationship between smoking and cancer of the lung. At that time the main evidence came from some 20 retrospective studies in 9 countries and 3 prospective studies. The important results of the individual studies are shown in tabular form. In addition to the "cause and effect" interpretation of this relationship various other explanations have been considered, not only by the investigators who carried out the original work, but also by various other authorities. These alternative explanations are discussed in the present report in the light of the data which were available when it was written 2 years ago. Most of these arguments have appeared elsewhere, and as the report is a summary, it cannot be sensibly summarized further. Dr. Doll's review provides a very good critical assessment of the work done up to June 1958 and should be read in conjunction with various reports which have since appeared giving other data germane to the problem.

E. A. Cheeseman

EYSENCK, H. J., TARRANT, Mollie, WOOLF, My ENGLAND, L. **Smoking and Personality.** *Med. J.* 1960, May 14, 1456–60. [19 refs.]

In randomly selected areas of the United Kin 2,360 men aged 40–70 and of different smoking were asked to reply to a questionary designed to m their personality traits. Analysis of the answers a significant difference between non-smokers, medium and heavy cigarette smokers in the averag of extraversion (which increases with smoking) a rigidity (which decreases with smoking). The characters are uncorrelated in individuals. There w significant difference in neuroticism. Pipe smoker the most introverted group studied. The data the confirm the view that genotypic differences exist be smokers and non-smokers and between types of sm [In subsequent correspondence it is pointed ou these results do not make any more reasonable the t that lung cancer and smoking habits have a co genotypic cause. It remains to be shown that extra and non-rigid non-smokers have the same incide lung cancer as a similarly constituted group of sm (RYLE, A., *Brit. Med. J.*, 1960, May 28, 1652). A R. E. W. FISCHER (*ibid.*) wittily writes, we migh "that women who associate with men also tend to certain personality characteristics (*e.g.*, a liking for

This will, of course, help to discredit the hypothesis there is a *causal* connexion between association with and maternity."] *A. Bradford Hill*

DER, E. L. & HOFFMANN, D. **Some Practical Aspects of the Smoking-Cancer Problem.** *New England J. of Med.* 1960, Mar. 17, v. 262, No. 11, 540–45, 2 figs. [24 refs.]

om the result of laboratory studies the authors est the use of filter cigarettes which will give a lower of smoke condensate than non-filter cigarettes, the umption of only half the cigarette since the latter contains appreciably more smoke condensate than former, the avoidance of too frequent puffs which tantially increase the condensate and also of inhaling ly which leads to much greater absorption of the ensate by the lungs. From an interview with 304 s over the age of 40 they found that nearly half had ged to filter cigarettes but had not thereby signifily changed their level of consumption. On the other l of heavy smokers who complained of definite ptoms, usually a chronic cough, half reported an rovement in their symptoms on making the change lter cigarettes. *A. Bradford Hill*

DTSON, K. P. **The Pathologic Effects of Smoking Tobacco on the Trachea and Bronchial Mucosa.** *Amer. J. Clin. Path.* 1960, Apr., v. 33, No. 4, 310–17, 6 figs. [18 refs.]

istological examination was made of 150 lungs re- ed from white male patients dying, in the Veterans inistration Hospital, Seattle, of causes other than nsive pulmonary disease. Data on smoking habits, pation and place of residence were sought from the -of-kin. Such data as well as adequate histological sec- s were available in 100 of the cases and the analysis es to this group. Changes observed in the tracheo- nchial epithelium were classified under the 4 headings, significant change, basal cell hyperplasia, squamous aplasia, and atypical proliferative metaplasia. The uency and severity of change was found to be related ne number of cigarettes smoked. Thus 5 (24%) of the non-smokers showed substantial changes (squamous atypical proliferative metaplasia) compared with 8 %) of the 20 light or moderate smokers (under 15 rettes a day) and 27 (51%) of the 53 heavy or exces- smokers (16 or more cigarettes a day). The 6 cigar pipe smokers all showed the slighter changes of basal hyperplasia. No carcinoma *in situ* was observed. The na was the most frequent site of the metaplasia. Nor- mucous membrane was seen in 50% of the non- kers compared with 20% of the heavy smokers.
A. Bradford Hill

, F. J. C., SALAMAN, M. H. & COHEN, June. **Incomplete Carcinogens in Cigarette Smoke Condensate: Tumour-Promotion by a Phenolic Fraction.** (With an appendix on **The Production of Cigarette Smoke Condensate** by J. G. BURGAN.) *Brit. J. Cancer.* 1959, Dec., v. 13, No. 4, 623–33, 2 figs. on pl. [32 refs.]

30 mice were given a single application of 300 μgm. of DMBA (9, 10-dimethyl-1, 2-benzanthracene) to the dorsal skin and, after a 3 weeks' interval, submitted to twice weekly applications of the phenolic fraction of cigarette smoke condensate for 37 weeks. 65 papillomas and 1 carcinoma had then occurred. On the other hand no tumours, benign or malignant, appeared in a group treated with phenolic fraction only while the application of 300 μgm. of DMBA alone produced only 6, all of which were outside the treated area. The phenolic fraction of cigarette smoke condensate appeared therefore to have considerable tumour-promoting activity but no carcinogenic activity. In view of such results the correlation between smoking habits and lung tumour incidence may be determined, not primarily by the carcinogenic effect of tobacco smoke, but by its predominantly tumour-promoting action on the bronchial epithelium.
A. Bradford Hill

KREYBERG, L. **3:4-Benzpyrene in Industrial Air Pollution: Some Reflexions.** *Brit. J. Cancer.* 1959, Dec., v. 13, No. 4, 618–22, 1 fig. [17 refs.]

Investigation in the gasworks of Oslo and Bergen showed relatively very large amounts of 3:4 benzpyrene in the air *i.e.* relative to the amounts that are present in cigarette smoke. Yet according to general experience the risk of lung cancer among gas workers does not appear to be greatly in excess of the risk in the general population. Particle size might be important in influencing the amounts deposited on the bronchi but alternatively there may be no causative relationship between 3:4 benzpyrene and the development of lung cancer. Its role in this connexion is unknown and there is as yet no evidence that it is the active agent operating in cigarette smoking.
A. Bradford Hill

ROOT, H. D., AUST, J. B. & SULLIVAN, A., Jr. **Snuff and Cancer of the Ear. Report of a Case.** *New England J. of Med.* 1960, Apr. 21, v. 262, No. 16, 819–20, 1 fig.

The carcinogenic potential of tobacco derivatives has been demonstrated on the skin of mice but no such effects have been clearly shown in man. The authors, from Minnesota, report the case of a 58-year-old farmer who in accordance with a local North American Indian custom had placed snuff in his left ear daily to weekly for some 42 years. A squamous-cell carcinoma developed at the site. *A. Bradford Hill*

COURT BROWN, W. M., DOLL, R., SPIERS, F. W., DUFFY, B. J. & MCHUGH, M. J. **Geographical Variation in Leukaemia Mortality in Relation to Background Radiation and Other Factors.** *Brit. Med. J.* 1960, June 11, 1753–9, 4 figs. [22 refs.]

This is an elaborate study attempting to link up the incidence of leukaemia with background location—and other factors. It is mainly a background study and

for this purpose elaborate measurements had to be made in 4 of the 10 areas in Scotland chosen as foci for study; 2 districts were mainly granitic, and 2 mainly sedimentary rocks. Houses and flats as well as open spaces were tested for their radioactivity and with all such data collected they were examined to see whether any correlation existed between them and the mortality rates for the said areas.

Over the years 1939–56 the highest mortality was in Aberdeen, then Edinburgh, and the lowest in Glasgow. In Aberdeen the excess was due to acute leukaemia and chronic myeloid leukaemia; in Edinburgh it was due to chronic lymphatic leukaemia.

Three possible explanations of the increase of deaths in these centres are given by the authors. They are:— Better case-finding, high economic status and exposure to ionizing radiations. The last-named is discounted as a significant agent. It is stated that local differences in the average exposure to diagnostic radiography may be greater than the differences in background radiation.

S. Russ

WOOD, Eileen E. **A Survey of Leukaemia in Cornwall, 1948–1959.** *Brit. Med. J.* 1960, June 11, 1760–64, 1 chart. [14 refs.]

This is a remarkable survey carried out over the past 12 years, for it is a survey on a somewhat static population. The people do not move about much in Cornwall and record-keeping is easier on this account, and since 1948 has been greatly improved. No less than 11 types of leukaemia have been studied, with 4 outstandingly prominent types *viz*:—acute myeloid or lymphatic—chronic myeloid or lymphatic. The following comment is made on the claim of STEWART *et al.*, (*Lancet*, 1956, v. 2, 447) that X-rays used during pregnancy may induce leukaemia in the child:—"an inquiry into the X-ray status of the mothers of the leukaemia children was made. At the West Cornwall Hospital between 1942 and 1950, 391 pregnant women had abdominal radiographs; in addition there were 122 pelvimetries. These investigations have now been reduced to 1 or 2 annually.

"At the obstetric centre at Redruth a survey has been made of all pregnant women undergoing X-ray examinations between 1948 and 1959. Records of 1,175 women were scrutinized and 200 pelvimetry estimations were noted. No mother of a leukaemic child has been found in either investigation."

The author discusses the bearing of economic status on the incidence of this disease which actually s no increase over the years studied.

[The report should prove of the greatest intere those engaged in or intending to pursue such stu

S. R

DAVIES, J. N. P. & OWOR, R. **The Diagnos Primary Carcinoma of the Liver. An As ment of the Reliability of Clinical Diagnos Uganda Africans.** *East African Med. J.* Apr., v. 37, No. 4, 249–54.

How reliable are the history and physical signs i diagnosis of primary cancer of the liver? In a population the answer will depend on how often one expect other conditions to produce progressive kn enlargement of the liver. The authors sought to a this question with regard to the population ar Kampala by examining the autopsy reports for a 9 period. Only cancer produced a clinical picture could be interpreted as primary hepatoma, an abscess and other causes of nodular enlargement very rare in the autopsy records. In 383 autopsies c was the cause of death, and these cancers includ examples of primary hepatoma, all causing nodula largement of the liver. There were 250 other ca judged capable of metastasizing to the liver, but in only 45 had done so. Only 38 of these cancers ne considered, since 7 were in children below the age when primary liver cancer is unknown. 17 showed tiny deposits, in 8 a primary tumour elsewhere clinically obvious, leaving 13 with occult or clin indefinable tumours; not all the latter, of course, v have closely mimicked hepatoma. In sum, ther there were 94 patients who had died with an enl knobbly liver without a clinically obvious cancer where, and in these the tumour was metastatic in at 13 patients. In this population therefore, as judg autopsy experience, clinical indications of primary cancer patients over the age of 12 are likely to be c in 8 out of 9 cases.

The relative infrequency of liver metastases, when the primary was in the intestinal tract, e comment. Much of the discrepancy was accounte by the small number of cancers of the stomach, pan and gut in this series (48 cases in all, 18 with secondaries); but part was felt to be due to the ten in Africans for death to occur from the direct effe the primary growth.

Alan B. Ra

DENTAL HEALTH

WIG, T. G., HEALY, W. B. & LOSEE, F. L. **An Association between Dental Caries and Certain Soil Conditions in New Zealand.** *Nature.* 1960, May 28, v. 186, 695–6. [10 refs.]

1955 it was "reported that a relationship exists een prevalence of caries and certain soil conditions ew Zealand" and a phase of the general investiga- of this observation now being conducted involves y of recent saline soils at Napier, Hawke's Bay. A r earthquake in 1931 in this area "resulted in the ting of a land mass some 60 miles long and at least iles wide to heights ranging up to 9 ft.". The saline exposed have been brought into production and for residential development. The preliminary results ıvestigation in this area are presented in this report.

1954–55 dental examinations of children were ed out in Napier and in Hastings, cities which are parable in size, climate, socio-economic conditions mineral composition (fluoride 0·15 p.p.m.) of their r supplies. The findings were that the Napier ren aged 5–8 years had a considerably lower caries experience than the children of equivalent age in Hastings. Details of the dental findings are described and set out in a table. Repeated in 1957 when fluoridation of water in Hastings had been carried out for 2½ years dental examinations showed caries prevalence in the 2 cities to be about equal.

Soil analyses in the 2 areas revealed definite differences in *p*H 5·7 to 6·7 in Hastings and in Napier from *p*H 6·4 to 8·1. In 3 soils with *p*H of over 7·5, shell fragments were present and the calcium carbonate content was 2–3%.

Spectrographic analysis of ash of various edible vegetables showed notable differences in trace elements for in general Napier vegetables were higher than Hastings vegetables in molybdenum, aluminium and titanium and lower in copper, manganese, barium and strontium.

There is reference to the literature on high molybdenum levels in soil and water in association with low caries prevalence. Much further study is required but it is suggested "At present it seems possible that a higher intake of molybdenum may be the prime factor responsible for the lower prevalence of dental caries among Napier children". *M. E. Delafield*

MENTAL HEALTH

ERTS, Nesta. **Everybody's Business. The 1959 Mental Health Act and the Community.** 28 pp. 1960. London: The National Association for Mental Health, 39, Queen Anne Street, W.1. [1s.6d.]

his cheap and excellent booklet is written in popular uage by a lay woman for lay people. As Lord ERSHAM says in a foreword it "deals with the oppor- ies now given to local authorities, voluntary bodies the man in the street to play their part in bringing ıt a new, hopeful era of development and under- ding for the sick in mind".

n appendix summarizes the Mental Health Act, 1959, the body of the booklet deals with certain miscon- ions about it which have arisen such as that a flood of ents is about to be discharged from mental hospitals. he author explains that most mental patients are com- tively harmless and can live in the community pro- d that they have some supervision and that they or relations have access to skilled advice at a day ital or psychiatric out-patient department. Special ngements need to be made for patients recently dis- ged from hospital and there must be close liaison veen the staffs, medical and lay, of hospitals and local orities.

n essential is the education of the public about what tal sickness really is.

he new proposals are by no means untried and what been done, in some cases for years, by certain local authorities is described. They include Birmingham, Oldham, Nottingham, York and Leeds. The pioneer efforts centred on the Graylingwell Hospital, Sussex, and the Stepping Stones Club at Bromley are set out.

Hints are given on the best way to run hostels for ex-patients or for the subnormal, social clubs, junior training centres, adult centres and special care units. Many patients can be employed in gainful occupations if care is taken in their selection.

The most pressing need, however, is to find staff. They must have proper training either before or after entering the service. It is wiser to delay development rather than to start with staff who are inadequately prepared.

The booklet is admirably suited to its purpose.

Allen Daley

DE LA MATA, R. C., GINGRAS, G. & WITTKOWER, E. D. **Impact of Sudden, Severe Disablement of the Father upon the Family.** *Canadian Med. Ass. J.* 1960, May 14, v. 82, No. 20, 1015–20.

An intensive study was made of 8 families (38 persons) under stress "specifically that due to disablement of the father" and the findings are reported "in a greatly abbreviated form". "The main object of the study was to investigate the effect of the disablement of the father on the equilibrium of the family, and the mechanisms employed to restore it". In the families chosen for study the disablement of the father was sudden and the degree

of recovery was not above 70% of his former capacity. The disablement had occurred not more than one year before the study was begun. The age of the fathers was between 20 and 50 years. In the investigation all members of the families were interviewed separately and the same interviewer later visited the families at home to obtain information about family interaction. No psychological testing was carried out.

The stories of these 8 families are well told with some discussion of the factors which may operate in sec a greater or lesser extent of adjustment to altere cumstances.

Among the conclusions it is said "The most s endeavours to rehabilitate the disabled person phys may be doomed to failure if insufficient attention is to his emotional state" and "It is highly desirab enlist the services of a psychiatrist in the rehabili process". *M. E. Delafi*

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

HÜRNY, T. Überprüfung der Erfolge der Trinkwasserfluoridierung in den USA. [**Evidence of the Success of Fluoridation of Drinking Water in the U.S.A.**] *Bull. Schweiz. Akad. Med. Wiss.* 1960, May, v. 15, No. 6, 451–64.

The English summary appended to the paper is as follows:—

"I had the opportunity to see with my own eyes the improvement in the dental caries resistance when examining small groups of children in the districts of *Newburgh/Kingston* (N.Y.) and *Grand Rapids/Cannonsburg* (Mich.). Since 1945 *Newburgh* (N.Y.) and *Grand Rapids* (Mich.) have fluorized their drinking water. To compare the results of these examinations I also examined groups of children of the towns of *Kingston* (N.Y.) and *Cannonsburg* (Mich.) where the water supplies are fluoride-deficient. After the dmf- and the DMF-index a caries reduction of 78·84% and 71·77% in *Newburgh* and 68·75% and 65·47% in *Grand Rapids* has been found. Spots on enamel caused by fluorine appeared rarely and only in a very unimportant form without any influence on the beauty of the teeth. All reliable scientists and health organizations have denied that the human body is injured by chronic fluorine intake with the drinking water in the recommended amount of 1 mg/l. They deny the damage not only for the districts with artificially fluorized water, but also for areas with the same and more but natural content of fluorine in the water. According to these scientists and public health men, we need not expect damage in the future.

"The fluoridation of public water supplies is considered by the *U.S. Public Health Service*, the *State Health Departments*, the *American Medical Association*, the *American Dental Association* and many other health groups to be the only possibility to bring under control this widespread disease of dental caries. After having made extensive tests, all these agencies recommend the fluoridation of public water supplies."

UNITED STATES DEPT. HEALTH, EDUCATION & WEL **Swimming Pools. Disease Control through per Design and Operation** [MICHAEL, J. M.] *Health Service Publication No. 665. CDC Tra Manual.* 1959, pp. vi + 147, 11 figs. Wash U.S. Govt. Printing Office. [$0.75.]

This training manual was first issued in early with revised editions in late 1954 and 1955. This e "represents the latest information on design, con tion, operation, maintenance, and the effect of eac disease control practices". It is intended to serve training and reference guide for State and local p health personnel and will, it is hoped, be useful i development of training programmes for operator owners of swimming pools.

The publication is in mimeographed form and co a mass of information and suggestions clearly se with diagrams, figures and illustrations. It begins an outline of a suggested short course of instructi last 3 days. There follows a number of sections inc in which are outlines of lectures on (1) swimming sanitation, (2) construction and remodelling a p swimming pool and bathhouse, (3) operation and m nance, (4) testing swimming pool water for chlorine dual and *p*H and (5) inspection of pool installation bacteriological sampling of public swimming pool w

Each lecture outline contains a large number of graphs or headings on subjects which could not a included adequately in a single lecture but will great value to the instructor to enable him to dete the points to emphasize. The headings are mainly statements of important aspects without detailed cription.

Included in this manual are report forms, a chec of questions to be answered as a means of rating a references to the literature, a list of instructio equipment and an index. *M. E. Delafi*

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

:, P. C. G. [B.Sc., S.M., M.I.C.E., M.I.W.E., M.Inst.S.P., F.R.S.H.] [Edited by.] **Waste Treatment. Proceedings of the Second Symposium on the Treatment of Waste Waters, organized by the Public Health Engineering Section, Department of Civil Engineering, University of Durham, King's College, Newcastle upon Tyne, 14–19 September, 1959.** pp. xii + 477, illustrated. 1960. London. New York. Paris. Oxford: Pergamon Press Ltd., Headington Hill Hall. [84s.]

1957 the Public Health Engineering Section of the artment of Civil Engineering of King's College in the versity of Durham organized a two-week Symposium he whole field of waste-water treatment [this *Bulletin*, , v. 33, 497]. The success of this meeting has led to organization of a second symposium on 2 aspects only vaste treatment: the theory and practice of biological tment, and the disposal of solids removed from liquid es. At this symposium held in Newcastle in 1959 180 participants from Britain and overseas attended. 21 papers presented are published in this volume edited discussions.

NTRODUCTORY

me Aspects of the Biochemistry of Aerobic Organic te Treatment by J. R. SIMPSON (pp. 1–30). This er contains a good review of the biochemistry con- ed in reducing the organic content of dilute organic es by aerobic biological treatment. There is descrip- of the chemical changes of breakdown and synthe- of organic compounds brought about by microbiologi- enzyme systems and the practical application of this wledge to the proper design and operation of biologi- waste treatment systems.

me Aspects of the Biochemistry of Anaerobic Diges- by J. R. SIMPSON (pp. 31–45). The chemistry of efaction and gasification is described with a consi- tion of the practical aspects of sludge digestion which uld be controlled by laboratory analyses and attention uch points as loading, temperature, seeding and pre- ion of excessive scum formation.

Discussion of these 2 papers is on pp. 46–51.)

cology of Activated Sludge and Bacteria Beds by A. HAWKES (pp. 52–97—discussion pp. 97–98). This paper with its many illustrative figures and numer- references contains a review of much of knowledge iving matter—bacteria, fungi, protozoa, the smaller azoa and macrofauna—which may be found in acti- d sludge and bacteria beds, the environments of ch are compared. The changes in the character and inant organisms in a sludge brought about by rent factors are described. The practical applications cological principles are discussed.

he Use of Manometric Methods in the Study of age and Trade Wastes by D. JENKINS (pp. 99–121, ussion pp. 121–125). The history of the methods of ct absorption to measure the oxygen-demand of ge are described from probably the first attempt by NEY (1908) which was followed by modifications and rovements and later the use of Warburg and Barcroft respirometers and the more recent development of large-volume respirometers. There are a number of illustrative figures and an account of some of the valuable work done with these methods.

II. BIOLOGICAL TREATMENT PRACTICE

New Developments in the Application of Kessener Brushes (Aeration Rotors) in the Activated-Sludge Treatment of Trade-Waste Waters by A. PASVEER The Hague (pp. 126–153, discussion pp. 153–155). In this paper there is a report on researches that have been carried out on the brush-aeration system which has found application particularly in the Netherlands and also in a few parts in Britain. There are many technical details and also some photographs of the system.

Process Design of Biological Oxidation Systems for Industrial Waste Treatment by W. W. ECKENFELDER and J. MCCABE of Manhattan College, New York, (pp. 156–185, discussion pp. 186–187). The authors here present a long mathematical presentation of the "relationships between BOD removed and biological sludge growth during the various phases of biological oxidation" and discuss a number of points or "concepts" the application of which are illustrated by an example of the design of a biological oxidation system.

The Application of Recirculation to the Purification of Sewage and Trade Wastes by C. LUMB (pp. 188–202, discussion pp. 202–205). "The term 'recirculation' in this context implies the dilution of the feed to a biological percolating filter bed with treated liquor which has already been through a biological purification process". The development of the process of recirculation, its technique of application, its value and the possible factors in its mechanism are described.

The Treatment of Chemical Wastes by I. S. WILSON (pp. 206–222, discussion pp. 222–225). Much detailed information is given here of the experience of Monsanto Chemicals Limited at its Ruabon factory where activated-sludge and sand-filter plants have effected an exceptionally high degree of purification of its noxious wastes. The chemicals produced at the factory include synthetic phenol, salicylic acid, aspirin, phenacetin, phthalic anhydride and numerous products for rubber processing.

The Treatment of Distillery and Antibiotics Wastes by C. J. JACKSON (pp. 226–237, discussion pp. 237–239). This short paper contains an account of the great and particular difficulties in the treatment of distillery and antibiotics wastes which may account for more than 90% of the original raw materials employed. There is a description of the various methods of treatment or disposal which are in use and of biological methods used abroad.

III. SAMPLING AND ANALYSIS

The Relevance of Waste-Water Analysis to the Design of Process and Pretreatment Plant by F. G. BROUGHALL (pp. 240–247).

Analytical Tests in Relation to the Discharge of Trade Effluents to Sewers by S. H. JENKINS (pp. 248–264).

The Effects of Liquid Wastes on Receiving Waters by R. J. H. DYSON (pp. 265–274).

In these 3 papers which were discussed as a whole (pp. 274–280) the significance of the analysis of a trade effluent is dealt with from the point of view of the industrialist and the officers of River Boards and Local Authority Sewage Works. The main methods of analysis which have particular reference to trade wastes are those of the Ministry of Housing and Local Government [this *Bulletin*, 1957, v. 32, 355], the Association of British Chemical Manufacturers and the Society for Analytical Chemistry (*Recommended Methods for the Analysis of Trade Effluents*, Cambridge 1958. W. HEFFER) and the American Public Health Association [this *Bulletin*, 1955, v. 30, 732].

The Self-Purification of Streams and the Relationship between Chemical and Biological Tests by E. LECLERC of the University of Liège (pp. 281–314, discussion pp. 314–316). This is an account of researches undertaken as part of a large programme of study of the actual state of many Belgian rivers. These researches were on temperatures and their influence on chemical and biological degradation of organic matter, dissolved oxygen consumption, nitrogen balance, biological analysis and toxicity to fish of crude wastes and particular substances. Examples of the application of the results of this research to a few rivers are given.

IV. SLUDGE TREATMENT

Principles of Vacuum Filtration and their Application to Sludge-Drying Problems by P. COACKLEY (pp. 317–332, discussion pp. 332–334). The older methods used in filtration experiments had shortcomings which are discussed. The author of this paper proposed some years ago the use of a theory of filtration (CARMAN, *Trans. Instn. Chem. Engineers*, London, 1938, v. 16, 168) which takes into account the major variables of applied pressure, filter area, the solids concentration and the viscosity of the filtrate. Some physico-chemical experiments on filtration are described and the results of these together with specific-resistance measurements can indicate the reasons for the difficulties in dewatering sludge.

Sludge Filtration and Drying by M. A. KERSHAW (pp. 335–346, discussion pp. 346–348). This short paper describes the stages in the process of sludge disposal which may include consolidation, digestion, chemical conditioning, drying, filter pressing and vacuum filtration.

Composting by J. C. WYLIE (pp. 349–360, discussion pp. 360–366). Composting, "a controlled process of decay which is effected by micro organisms which are indigenous to the wastes themselves" is here described under the headings of fermentation, mass composting, segregation, mechanical preparation of compostable materials, use of sewage sludge, batch composting, multistage composting in vertical silos and continuous composting by the Dano process.

The Practice of Sludge Digestion by J. GRIFFITHS (pp. 367–378, discussion pp. 379–384). This is a general account of sludge digestion, its history, its problems and its modern developments. Among the subjects considered are the effect of temperature, seeding and mixing, water content of sludge, gas production and utilization, tank design, laboratory control, effect of toxic substances anaerobic treatment of industrial wastes.

V. WASTE TREATMENT: PARTICULAR INDUSTRIES

The Origin, Treatment and Disposal of Effluents in Food Canning and Freezing Industries by D. DICKI (pp. 385–395, discussion p. 396). Wastes from cann and freezing factories are similar to domestic kit wastes and some information on the sources of effl in canning carrots and wastage in preparation of fruit vegetables is given in illustration. Pretreatment of s vegetables is of value in lessening the amount of s in the effluent. In purification the first essential is e tive screening, after which the effluent can usuall discharged into a sewer. Biological purification met have been used for cannery wastes. There is a discus of the spray-disposal method in which the effluer distributed as a fine rain on land covered by an es lished cover crop.

The Application of Biological Processes to the T ment of Liquid Tannery Effluent by G. H. GREEN 397–407, discussion pp. 408–410). This short paper g a list of the organic materials and chemicals which be present in effluents from tanneries. No great tec cal difficulty exists in removal of BOD and colour f spent vegetable-tan liquors but of the chemicals n tioned alkali (lime or caustic), sulphide and chrom may be present in sufficient quantity to interfere biological processes of purification.

Treatment of Waste Waters from Milk-Products tories by A. B. WHEATLAND (pp. 411–426, discussion 427–428). This paper, which is published by permis of the Department of Scientific and Industrial Resea contains much detail of the character of milk wastes the stages in the various processes of purificatio which they are subjected in order to give satisfac results.

VI. RECLAMATION

Reclamation of Water from Domestic and Indus Wastes by P. H. MCGAUHEY, University of Califo (pp. 429–439, discussion pp. 439–442). This is an inte ing paper in which the author discussed the factors w have continued to delay development of water recla tion from sewage. "These include psychological siderations, together with inertia, lack of technical kn ledge and a reluctance to separate the reclamation disposal aspects of sewage purification". A consider number of examples are given of the reuse of sew plant effluents in the United States for the purpose irrigation of crops and playing fields and for us mining, oil-refining and other industries. Researc reclamation has progressed greatly and it is st "There is, therefore, reason to believe that in the decade use of water reclaimed from sewage will bec common practice".

Each paper in this valuable and well-produced bo followed by a list of the relevant literature. The b has an excellent subject index, an author index and a of the lecturers and participants in the Symposium.

M. E. Delafie

ATMOSPHERIC POLLUTION

BENS, B. D. **Five Years of Continuous Air Monitoring.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 39–45, 5 figs. [10 refs.]

ir was sampled almost continuously from May 1954 April 1959, by using an AISI smoke sampler MEON *et al., Instruments,* 1953, v. 26, 566) 80 feet ve street level and 290 feet above sea level, in a resi- ial area in Berkeley, California. Pollution is ex- sed in COH/1000 ft. [see HEMEON *et al.*, this *Bulle-* 1959, v. 34, 466].

he author discusses the results, using the probability roach (see *Public Health Service Publication* 637, , U.S. Dept. Health, Education and Welfare, Cincin-) to compare different periods, and concludes that pt on very clear days most data can be combined by probability methods: the year 1958–59 was however exception. There seems to be no consistent trend in ual average pollution, although motor traffic has dily increased. Seasonal, monthly, weekly and daily ation are discussed. *John McK. Ellison*

ERNAT. J. AIR POLLUTION. London. 1960, Mar., v. 2, No. 3, 201–82, numerous figs. [Numerous refs.]

Symposium on Polycyclic Hydrocarbons. Papers presented at Air Pollution Symposium, American Chemical Society, Atlantic City, 17 Sept. 1959.

he 6 papers presented at the Symposium were almost rely concerned with the development of analytical hods for separating, identifying and quantitatively ermining polycyclic aromatic hydrocarbons.

he first paper presented was by H. L. FALK, P. KOTIN A. MILLER (*Aromatic polycyclic hydrocarbons in luted air as indicators of carcinogenic hazards,* 201–209).

hey suggested as the elution conditions in the lung for ycyclic aromatic hydrocarbons found in soot are very erent from those of the laboratory, a method for the lysis of the hydrocarbons should be used, based on ion of the soot with an aqueous protein solution. ey proved experimentally that the conditions in the g were different, by showing that benzene extracted hydrocarbons in particles down to 40mμ diameter le an aqueous protein solution extracted only particles er than 100 mμ. They determined their hydrocarbons means of a chromatographic separation on de- vated alumina followed by absorption and fluores- ce spectroscopy. Some good spectra have been ob- ed by these techniques for a number of known rocarbons and several as yet unidentified compounds. ey suggest that as there is a marked structural simi- ty between carcinogenic and non-carcinogenic hydro- bons there is competition at the site of action for our production. They have shown experimentally that e of the non-carcinogenic or weakly carcinogenic drocarbons can act as inhibitors for the production of ours.

The second paper was presented by J. F. THOMAS, B. D. TEBBENS, E. N. SANBORN and J. M. CRIPPS (*Fluorescent spectra of aromatic hydrocarbons found in polluted atmosphere,* pp. 210–220).

They have investigated the possibilities of fluorescence spectrometry as an analytical tool for the detection of polycyclic aromatic hydrocarbons. They find that the method is readily adaptable to minute amounts of hydrocarbons. They examined the fluorescent spectra of solutions of hydrocarbons and those produced directly from paper chromatograms of separated hydrocarbons obtained from polluted air. The possible use of the method in quantitative analysis was investigated.

The third paper was by G. E. MOORE and M. KATZ (*Polynuclear aromatic hydrocarbons in the particulates of diesel exhausts in railway tunnels and in the particulates of an urban atmosphere,* pp. 221–235).

They describe the identification of polynuclear hydrocarbons in the tunnel air in which heavy Canadian diesel locomotives operate. The results obtained showed that although the particulate loading of the tunnel air was 8 times the loading of the general urban atmosphere, the amounts of hydrocarbons were such as might be found in the tunnel ventilating air. (No actual figures showing concentrations of hydrocarbons in the tunnel are quoted.) The hydrocarbons extracted from the soot were chromatographically separated on columns of alumina and identified and quantitatively determined by absorption spectrophotometry.

The next paper was presented by L. DUBOIS, ANN CORKERY and J. L. MONKMAN (*The chromatography of polycyclic hydrocarbons,* pp. 236–252).

They describe a method of analysis for mixtures of pure polycyclic aromatic hydrocarbons and those present in polluted air. The method consists of separating the hydrocarbons first on columns of alumina and then on sheets of acetylated paper. The separations obtained on the paper were much better than those by conventional absorption chromatography. In order to identify the hydrocarbons, the chromatograms were examined by absorption and fluorescence spectroscopy.

Then follows *Ultraviolet, visible and fluorescence spectral analysis of polynuclear hydrocarbons* (pp. 253–272), by E. SAWICKI, T. R. HAUSER and T. W. STANLEY.

They quote the wavelengths of the main absorption maxima in pentane, the main activation and fluorescence maxima in pentane and sulphuric acid of a number of polynuclear hydrocarbons. Using this data they have developed techniques for the detection of a number of hydrocarbons in complex mixtures.

The last paper was presented by E. SAWICKI, W. ELBERT, T. W. STANLEY, T. R. HAUSER and F. T. FOX (*The detection and determination of polynuclear hydrocarbons in urban airborne particulates—1. The Benzopyrene fraction* (pp. 273–282).

By means of a chromatographic separation on an alumina column followed by absorption and fluorescence spectroscopy benzo(a) pyrene has been determined in the air of 9 American cities. *B. T. Commins*

RONDIA, D. L'incidence des brouillards de février 1959 sur la concentration en hydrocarbures polycycliques de l'atmosphère de la région liégeoise. [**The Effect of Fog in February 1959 on the Concentration of Polycyclic Hydrocarbons in the Air of Liege**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et méd. Légale.* 1960, Mar., v. 18, No. 3, 220–27, 1 fig.

Investigations showed a 4–6-fold increase in polycyclic hydrocarbons during the fog period, especially in the centre of Liège.

CLAYTON, G. D., COOK, W. A. & FREDRICK, W. G. **A Study of the Relationship of Street Level Carbon Monoxide Concentrations to Traffic Accidents.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 46–54, 7 figs.

Previous workers have reported that CO concentrations too low to cause subjective symptoms affected physiological mechanisms and disturbed vision, hearing, speech and reflexes. The present study, carried out in Detroit, was intended to find out whether these in turn produced in drivers a proneness to road accidents.

Air was sampled at 4 sites and both this and the blood of accident victims was analysed for CO. The relationships between occupation and traffic accidents and between atmospheric CO inside a car and per cent carboxyhaemoglobin (COHb) are discussed.

The COHb value of 237 drivers, pedestrians and passengers involved in accidents are shown in a table. In 50% of drivers it was less than 3% saturation.

It is generally held that less than 10% saturation will not affect driving ability, and since only 3 out of 237 had values as high as this the authors conclude that in Detroit CO in the air does not increase accidents.

John McK. Ellison

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

LOGAN, W. P. D. **Occupational Mortality.** *Proc. Roy. Soc. Med.* 1959, June, v. 52, No. 6, 463–8 (Sect. Epidem. & Preventive Med. 19–24), 19 figs. [11 refs.]

The Chief Medical Statistician to the General Register Office has followed precedent and given a short selection of some outstanding features of the Registrar-General's Decennial Supplement on Occupational Mortality for 1949–1953, in a talk to the Section of Epidemiology and Preventive Medicine of the Royal Society of Medicine in February of last year.

He briefly sets out the indices which are used in computing occupational mortality, and the difficulty arising from discrepancies between the occupational descriptions in the Census schedules and those in the death registers. He then examines particularly the gradient of mortality with social class.

A steadily rising gradient in mortality from all causes from Social Class I to V, found previously in 1930–1932, has been replaced in 1949–1953 by a fluctuating or W-shaped line. Dr. Logan finds that after adjusting the data for changes in the composition of the social classes since the last census, and after allotting company directors to Social Class II instead of to Social Class I, the trend rises uniformly from I to V as before.

Diseases showing in the latest figures a strong upward trend in mortality from Social Class I to V are bronchitis, other myocardial degeneration, and both ulceration and cancer of the stomach. Duodenal ulcer shows a gradient in the same direction, but this is less marked and less regular. Among other cancers, the trend for cancer of the lung in men is upward from I to V with some irregularity, but downward for women. Cancer of the lip shows remarkable contrasts between different socio-economic groups: the Standardised Mortality Ratio for agricultural workers is 359, some twenty times as great as that of clerks, 16. Cancer of the breast and cancer of the uterine cervix show opposite trends with social class, the first falling and the second rising from Social Class I to V. Frequency of childbearing is a common explanation, but this hardly accounts for the emergence of the same pattern in single women. Similar contrasts between these two cancers appear in their local distribution, which appear in the Registrar-General's parallel volume on Area Mortality. [Do these reflect differences in the Social Class composition of different areas?]

In men, coronary disease shows at all ages a pronounced downward trend in mortality from Social Class I to V. In women this trend only appears after the age of 65: in younger women each social class appears to be equally affected by the disease. Deaths from poliomyelitis also show a steep downward trend from Social Class I to V, and selected occupations show great difference. The SMR of doctors is 800, while that of coal-miners is only 5 (1 registered death compared with 22 expected). Suicide in men presents an unusual V-shaped distribution, being lowest in Social Class III and rising at ea

end of the social scale. The trend in married women, on the other hand, is steadily downward from Social Class I to V.

[The data abound with baffling problems. Why has the social class gradient in mortality from bronchitis increased in the last 20 years? The high mortality from poliomyelitis among doctors is, with the risk of infective contact, understandable, but why are they closely rivalled by lawyers? Why the anomaly between men and married women in the social class distribution of suicide? Dr. Logan has admirably whetted the appetites of his original audience and of later readers. Many of them will want to study the complete publication of two volumes, although, as he implies, their enthusiasm may, at 7 guineas the set, fall short of actual purchase.]

A. S. Fairbairn

ARCH. MALAD. PROFESSIONNELLES. Paris. 1959, Sept.–Oct., v. 20, No. 5, 465–574. 5es Journées Nationales de Médecine du Travail. Lyon, 9–10–11 octobre 1958. 1er rapport. Reclassement professionnel des tuberculeux pulmonaires. **[The Rehabilitation of Patients suffering from Pulmonary Tuberculosis.]**

The fifth national conference on Occupational Medicine was held at Lyons from 9 to 11 October, 1958. The first subject presented for consideration was the rehabilitation and resettlement of patients suffering from pulmonary tuberculosis.

J. GERMAIN. *Problems of the rehabilitation of patients suffering from pulmonary tuberculosis. A general and medical survey* (*pp.* 465–478).

The rehabilitation and resettlement of persons disabled from any cause is a major concern of doctors in industry. Tuberculous patients present peculiar difficulties because the disease is chronic and despite vigilant medical and social supervision liable to exacerbations and relapses. While there have been great advances in the diagnosis and treatment—medical and surgical—of the disease it is too readily assumed that pulmonary tuberculosis has been conquered. The fact is that though fewer persons die from the disease, an increasing number, owing to modern treatment, recover but are handicapped in varying degrees for life. This creates problems of their future employment.

The primary aim of rehabilitation should be to fit the workman to return to his previous job. Rehabilitation is not to be regarded as a phase which follows treatment; it should commence from the very date of admission to sanatorium and continue progressively throughout the life of the patient.

Dr. Germain recorded his experience over a period of 10 years, 1946–1956, of training courses of 15 months' duration under his direction at Mangini Sanatorium at Hauteville-Lompnes. The patients—500—were all females suffering from chronic tuberculosis of the lungs. The success of the scheme is proved by the fact that 85% of the candidates obtained a diploma and more vacancies for work were offered than the school could fill.

[This contribution has great merit; it reveals a physician with a missionary zeal not only to fit his patients for a job but to regain self-respect and joy in living. The problem—as is so often emphasized—is not tuberculosis but individual men and women afflicted and handicapped by it. Furthermore resettlement is not the end of the endeavour, there must be unremitting, continuing, progressive supervision. This calls for close co-operation between the patient, his employer, fellow-workers and doctors and social workers.]

R. BAILET. *The management of patients with arrested or cured tuberculosis, from the rehabilitation aspect* (*pp.* 479–498).

Rehabilitation of disabled persons, including tuberculosis patients, is not a new problem. It has existed throughout the present century and a great impetus to the movement was given by the wars of 1914–1918 and 1939–1945. [In Great Britain this was marked by the King's Roll of the Disabled, 1919, and the Disabled Persons Employment Act, 1944. Papworth and Preston Hall tuberculosis colonies became household names.]

Dr. Bailet reiterated that rehabilitation must not be regarded as an end in itself; the process is incomplete without successful resettlement in employment suited to the physical, mental and social capacity of the workman. General training is not enough; the patient must be prepared for work in which there are openings and assured employment. Nominal jobs based on the emotional reaction of sympathetic employers is not a satisfactory approach because these jobs flourish only in times of full employment and terminate in periods of slump when even fit men are out of work. The retraining of the handicapped workman must ensure a high degree of competence and the higher his skill the more likely he is to obtain employment and to hold it. Placement of the tuberculous workman is difficult because many employers still regard him as unprofitable and fellow-workmen fear contact infection.

Until now private philanthropic organizations have endeavoured to show the way; the time has come when the Government must accept the responsibility and develop a national scheme.

R. COOREMAN. *The retraining and resettlement of tuberculous patients in the Lyons area (pp. 499–515).*

In the Lyons area there are 7 training centres. Of these three are for women and provide instruction in secretarial work, tailoring, machine operating and several other skills. At the 4 centres for men the training embraces a wide range of occupations including watch and clock repairing, machine turning, carpentry and industrial design. In addition there are 3 special schemes, for severely handicapped, including a sheltered workshop at Annecy.

The staff made a special study of the causes of relapse. Among the important causes named are too early resumption of work and jobs beyond the physical and medical capacity of the individual patient.

G. DESPIERRES and C. OLLAGNIER. *Return to work of the tuberculous patient as seen by the physician in charge of city hospital* (*pp.* 516–523).

The preceding papers were concerned with patients

treated in sanatoria in the country. Many patients, however, refuse to go into sanatorium and so are treated in the chest units of general hospitals in the cities or in their homes. The problems of retraining and resettlement differ considerably in these diverse situations. In hospitals retraining is virtually impracticable and so the main purpose must be to restore the patient for work with his previous employer. This objective could be greatly advanced through governmental schemes.

Following the 4 main papers a series of contributions were presented recording the experience of doctors in particular industries; gas and electricity, building trade and public works, dock work and an electrical manufacturing company. Reference was also made to the special problems of young persons and cases of non-pulmonary tuberculosis.

[It emerges that the relevant problems in France con form closely to those in other industrial countries. Th approach too is similar but Government schemes hav been later in development than in Great Britain. However for the future France is in a very favourable positio through having a national Occupational Health Service This could ensure integration of the work of doctors social workers and others for the benefit of individua patients. Periodical X-ray examination as part of genera medical supervision would assist early diagnosis of nev cases and of relapse in known cases.]

A. Meiklejohn

OCCUPATIONAL PHYSIOLOGY

WRIGHT, B. M. & MCKERROW, C. B. **Maximum Forced Expiratory Flow Rate as a Measure of Ventilatory Capacity with a Description of a New Portable Instrument for measuring it.** *Brit. Med. J.* 1959, Nov. 21, 1041–7, 7 figs. [16 refs.]

Although there is some disagreement about the most suitable interval of expiration over which to measure volume, all are agreed that a single-breath estimate is preferable to the exhausting, multibreath maximum-voluntary-ventilation as an estimate of ventilatory capacity.

The peak-flow meter described here measures the highest flow rate sustained for at least 10 milliseconds during forced expiration (PFR). It operates on "the variable area orifice meter" principle and does not require elec tricity supply. Sterilizable or disposable mouth-piece can be used.

Extensive calibration and user trial data are given. A correlation coefficient of 0·86 was found in a small adul group between PFR and Forced Expiratory Volume The average PFR for young miners was over 700 litre per minute; flows below 50 litres per minute wer obtained in elderly, disabled women.

The instrument is claimed to be a simple and reliabl device for measuring the maximum expiratory flow rat during a forced expiration which, it is believed, is stable and useful measure of ventilatory capacity.

M. L. Thomson

OCCUPATIONAL DISEASES

SUTHERLAND, C. L. **Pneumoconiosis—its Effects and Complications. The Wyers Memorial Lecture, 1959.** *Trans. Ass. Indust. Med. Officers.* 1960, Apr., v. 10, No. 1, 4–15. [Numerous refs.]

Dr. Charles L. Sutherland delivered the third Wyers Memorial Lecture at a meeting of the Association of Industrial Medical Officers in London on 30th October, 1959. The presentation of the subject, he states, is from the angle of those who have to diagnose the disease and to assess the disablement it causes. This is the function of the Pneumoconiosis Medical Panel of the Ministry of Pensions and National Insurance (MPNI). To his task Dr. Sutherland, formerly chief medical officer of the Silicosis Medical Board and later senior medical officer on the headquarters staff of the MPNI, brought the mature experience and wisdom of practice extending from the original Workmen's Compensation (Silicosis) Act, 1918, to the National Insurance Industrial Injuries Act, 1946. He reveals the scrupulous care and thought which has been directed to define a *via media* betwee generally accepted facts about pneumoconiosis, i effects and complications, and the published results c current research on outstanding problems so as to assu to individual claimants for benefit (compensation) justic within the law.

The lecture will be of interest to readers all over th world as reflecting the official attitude in Great Britai to the diagnosis and assessment of the disease for com pensation purposes. Instead of presenting this abstra as a narrative, it seems preferable for the benefit of tho who cannot easily consult the original to provide th substance of the lecture in a series of quotations wi comments in parenthesis where necessary. As far possible care has been taken to ensure that no excerpt out of context.

Definition

Under the National Insurance Industrial Injuries A (1946) "Pneumoconiosis means fibrosis of the lungs d

to silica dust, asbestos dust or other dust and includes the condition known as dust reticulation [Byssinosis is not included in this definition]."

Diagnosis and Assessment

"The silicotic nodule is hard to the touch, it projects above the cut surface and is most profuse in the upper parts of the lung. The lung tissue between the nodules is functionally healthy. In the pneumoconiosis of coalminers [coalworkers], the changes are similar to but more extensive than those of the town dweller. A standard for diagnosis must therefore be adopted. Dust foci sparsely distributed and soft to the touch are not diagnostic of a disease. When the foci are more numerous and palpable we may consider the condition as a pneumoconiosis."

"It is frequently stated that the radiograph does not give any indication of the extent of disability. Massive shadows, however, are often associated with much disablement, and they certainly mean a more serious prognosis."

"Category 1 [Geneva Classification, 1958, this *Bulletin*, 1960, v. 35, 21] represents a minimal change at most and it is not at present recognized as disease for benefit purposes. The recognition of Category 2 is therefore important on several counts. For example it has been stated that massive shadows do not appear unless on a background of Category 2. This is a doubtful assumption."

[Category 1 pneumoconiosis of coalworkers is, as Dr. Sutherland admits, important in miners under the age of 30 years. Does Category 1 accompanied by tuberculosis constitute the disease as defined? This is pertinent if Caplan's syndrome is accepted as the disease as it is remarked that it may occur without a background of discrete opacities. And what of silicosis Category 1; is this disease or not?]

"The amount of disablement in simple pneumoconiosis is not great till later in life when other troubles contribute to the disability. Pneumoconiosis of the discrete type is not likely to cause death by itself, nor does it appear to shorten life."

There is "no radiographic evidence that the specific opacities of simple pneumoconiosis disappear with the development of emphysema."

"In assessing disability in practice, a diagnosis of pneumoconiosis [Cat. 2 Geneva Classification] leads to an assessment of what is in effect 10% even if no disablement is detected."

"Massive fibrosis frequently produces right ventricular hypertrophy, simple pneumoconiosis rarely does so."

"Signs of involvement of the right heart are not common in simple pneumoconiosis, but it may occur occasionally."

"All the evidence that can be obtained does not point to strain on the right heart or to anoxia arising from the presence of simple pneumoconiosis."

"There is much truth in the statement that the day is far distant when readings from a machine will supersede clinical observation."

Pneumoconiosis and Tuberculosis

"The diagnosis of tuberculosis is based on the presence of the tubercle bacillus in the sputum, or very definite evidence clinical and radiographic of active tuberculous lesions."

"The diagnosis of pneumoconiosis in the presence of active tuberculosis is more difficult; and much will depend on an adequate industrial history [this emphasizes the importance of personal experience of previous cases in particular occupations, processes and environmental conditions]."

Bronchitis and Emphysema: Pulmonary Disability

"Once bronchitis has been established there is an intolerance for dusty and smoky atmospheres. . . . . This intolerance does not mean that dust or smoke is the cause of bronchitis."

"If bronchitis and emphysema occur along with simple pneumoconiosis, it is at present assumed to be a separate condition, although it may increase the disability."

"The broken down breathless old collier presents a problem. What has produced his condition? The evidence that dust is the cause or even part cause is very slight, even the influence of the occupation itself is doubtful. The subject cries out for investigation: the remedy should be sought and applied before the victim's condition becomes a chronic irreversible one."

Asbestosis

"In this country [Great Britain] we find that clubbing of the fingers is common enough to constitute a diagnostic feature, that cyanosis appears in advanced cases, and that the condition progresses after exposure to dust has ceased."

"With a sound industrial history of exposure and the clinical findings a diagnosis may be made in the absence of definite X-ray findings."

"We believe that there is an association between the conditions [asbestosis and carcinoma of the lung]."

Among other topics dealt with are hypertension, right ventricular hypertrophy, coronary artery disease, spontaneous pneumothorax and radio-opaque dusts.

A. Meiklejohn

OSANAI, H. **The Penetration of Dust Particles introduced in the Alveolar Cavity into the Lymph Flow in Rats. The Stomata of the Lymph Vessels open to the Alveoli and the Types of Dust Penetration through the Alveolar Wall.** *Rep. of Inst. Sci. of Labour.* Tokyo. 1959, Mar., No. 54, 1–10, 10 figs. (8 on 4 pls.) [21 refs.]

In a series of experiments rats received intratracheal infusion of 3 gm. coal dust suspended in 100 ml. of 20% hypertonic glucose solution. This solution was used to dilate the pathways of dust transport in the lungs and to increase viscosity of the medium. The rats were killed 2 hours after infusion and the lungs were fixed in formalin. Serial sections were stained either with haematoxylin and eosin or with eosin alone. Lines of free dust were seen to penetrate through spaces between the epithelial cells of the alveolar walls and so into the perivascular and peribronchial lymphatics. In a few

sections openings were also seen between the cuboidal or cylindrical epithelial cells of the bronchi.

In a second series of experiments rats received intratracheal infusion of 3 gm. of coal dust suspended in 100 ml. of Ringer's solution. Rats were killed at daily intervals up to 8 days and then at 14 days after infusion. The lungs were fixed in formalin and then treated by *technique de congélation-dissolution* (L. Rison.) Serial sections were stained with haematoxylin and eosin. 24 hours after infusion most of the dust had been phagocytosed in the alveoli; the hilar glands contained only a few free dust particles and very few particles were seen in the perivascular and peribronchial lymphatics. After 2 days dust-laden phagocytes could be seen in the lymphatics. After 3 days dust-laden phagocytes were more numerous in the lymphatics and they could now be seen penetrating the perivascular and peribronchial walls. Processes from the phagocytes were inserted into spaces among the cuboidal epithelial cells. From 4 to 14 days after infusion there was a steady increase in the number of dust-laden phagocytes in the perivascular and peribronchial lymphatics with a corresponding decrease in the number of cells in the alveoli. Most of the dust is thus transported in phagocytes and only a small amount as free particles. The stomata can be regarded as part of the lymphatic system. [21 references are listed but only 4 are quoted in the text. No reference is made to Lambert's finding of broncho-alveolar communications.]

D. Rivers

RIVERS, D.; WISE, M. E.; KING, E. J.; NAGELSCHMIDT, G. **Dust Content, Radiology, and Pathology in Simple Pneumoconiosis of Coalworkers. Part I: General Observations** [RIVERS, WISE, KING & NAGELSCHMIDT]. *Brit. J. Indust. Med.* 1960, Apr., v. 17, No. 2, 87–93, 4 figs. **Part II: Detailed Analysis of the Data** [RIVERS & WISE]. *Ibid.*, 93–108, figs. 5–13. [22 refs.]

This is an important paper which should be studied in the original. In Great Britain this particular field of study has great potentiality in association with the Pneumoconiosis Field Research of the National Coal Board [this *Bulletin*, 1959, v. 34, 1129] and the routine periodical X-ray examination of all coalminers. The paper is in 2 parts, the first describes the methods and techniques and the general findings; the second part is a detailed analysis of the data. The investigation—it is important to note—was restricted entirely to simple pneumoconiosis among coalminers in South Wales. The criteria of choice of cases were availability of recent (within 2 years) radiographs, absence of tumour, tuberculosis and gross discrepancies between right and left lungs. Examples of the various types and severity of emphysema were included. None of the cases included showed macro- or microscopic changes suggesting silicosis.

The material consisted of coalminers' lungs obtained from 32 routine necropsies and 13 fatalities in pit accidents carried out by Professor GOUGH and his colleagues at the Welsh National School of Medicine, Cardiff. The radiographs were classified according to the Sydney Classification, 1950 [*ibid.*, 1954, v. 29, 626]. The carbon, quartz, mica and kaolin content of the lungs was det mined chemically. Gough sections [*ibid.*, 1948, v. 414] were used to assess the type and severity emphysema and the presence of fibrous dust nodul Histological sections, appropriately stained, were used grade the amounts of reticulin and collagen in t simple dust foci.

The mean weight of total dust, based on examinati of the right lung, increased with radiological category simple pneumoconiosis; category 0, 4·3 gm. and categ 3, 26·7 gm. but considerable overlapping between ca gories existed. Mineral matter and carbon contribut about equally to the radiological changes but, weight f weight, mineral contributed about 9 times more th carbon. A physical explanation for this is suggested terms of the relative absorption of X-rays by carbon a mineral. As there is abundant evidence that coal a silicates are relatively non-fibrogenic the hypothesis advanced that the radiological changes in simple pne moconiosis of coalworkers are produced by inert du and so depend only on the amounts of some or all t different dust components in the lung. This wou imply that the radiological changes are due to t amounts of coal and silicates in the lungs and not tissue reaction. [See also this *Bulletin*, 1950, v. 25, 47 476.]

A. Meiklejohn

WYATT, J. P., with the technical assistance of V. V FISCHER. **Morphogenesis of Pneumoconiosis occu ring in Southern Illinois Bituminous Worker** *Arch. Indust. Health.* Chicago. 1960, May, v. 2 No. 5, 445–57, 10 figs. [24 refs.]

Paper-mounted whole lung sections of the type intr duced by Professor GOUGH [this *Bulletin*, 1948, v. 2 414] are apparently not commonly made on the oth side of the Atlantic. 6 selected cases of bitumino coal workers were studied by this method. Judging the sections shown the amount of pneumoconiosis w not very great and death was not related to the lu condition.

The sections confirmed the observations of HEPPL STON [*ibid.*, 1948, v. 23, 336] that the dust forms a shea on the outside of the respiratory bronchiole. The du concentrations and the emphysema are found in t middle portions of the secondary lobule. This cent lobular situation of the emphysema with the disappea ance of the terminal bronchiole is a structural alterati found not only in bituminous and soft coal workers b also in emphysematous middle-aged males who have h no dust exposure. A comparison of these 3 types given in table form. Coal nodules were present in t bituminous cases, prominent in soft coal workers a rare in the purely emphysematous cases. In some of t workers from the Southern Illinois coal fields it w observed that the emphysematous state extended beyond its original site. This is not due to the mecha ical action of the coal at bronchiolar level; other facto are involved.

It is suggested that the stiffened dilated bronchi mechanically compresses or obstructs surroundi primary air lobular tissue thus interfering with the retu

air flow from neighbouring respiratory passages. In cases where the exposure to dust has stopped, the clearing of the coal from the lungs leaves a structural pattern of deranged lung which may sometimes be difficult to relate to an occupational hazard.

Charles L. Sutherland

SANDER, O. A. **Current Concepts of Pneumoconioses—Clinical Aspects.** *J. Amer. Med. Ass.* 1960, Apr. 9, v. 172, No. 15, 1587–90, 3 figs. [12 refs.]

A diagnosis of pneumoconiosis should not be made on the radiological findings alone; a detailed medical and occupational history is as important as other factors. The clinician's object is to relieve whatever symptoms and fears the patient may have and to take steps to prevent the pneumoconiosis becoming progressive. To do this he must know what the dust exposure has been; most medical directors and consultants to foundries have information from detailed dust surveys, as to the percentage of free silica in the dust inhaled. It may be that a nodular appearance on an X-ray film may disappear with time, being due possibly to a viral pneumonitis or a sarcoidosis with remission. The appearance of the film may be due to inhaled iron particles and where the root shadows are normal it is unlikely to be silicosis.

Smoking may be a major factor in the development of bronchitis, bronchiolitis and obstructive emphysema. Excessive smoking leads to impairment of the ventilatory capacity of the lungs. A detailed history of the smoking habits of the patient should therefore be taken in pneumoconiosis cases. In many cases with minimal silicosis it is unsafe to conclude that the silicosis is the major cause of the emphysema which may be present.

Charles L. Sutherland

PAUL, R., FLETCHER, G. H. & ADDISON, G. **A Comparative Study between Europeans and Africans in the Mining Industry of Northern Rhodesia.** *Med. Proc.* Johannesburg. 1960, Feb. 13, v. 6, No. 3, 69–74, 4 figs.

OOSTHUIZEN in 1958 [this *Bulletin*, 1959, v. 34, 50] described certain differences in the radiological appearances between the lung fields of Europeans and Africans in South Africa. He considered that the following features were important in differentiating the 2 racial groups.

In the African the diaphragm is flatter in appearance and higher in position, and the costo-phrenic angles are less acute. The cardiac silhouette is more transverse in position, creating the erroneous impression that the heart as shown by the transverse diameter is larger than in the European. The pulmonary striations are often more pronounced and tend to follow a more horizontal course as compared with the European, creating the erroneous impression of abnormal accentuation of linear lung markings and an appearance of false nodulation, as the result of vessels being seen end on. In the age-group over 40, a "gritty" appearance is often seen in Africans with no industrial history of work in a dusty atmosphere. These observations, if confirmed, would be important in the early diagnosis of pneumoconiosis among African labourers in the South African goldmines.

In the copper mines of Northern Rhodesia the Pneumoconiosis Medical Bureau had ample material to make a comparative study of the 2 racial groups. At this Bureau about 6,000 Europeans and 35,000 Africans are clinically and radiologically examined each year. A carefully planned survey was undertaken and radiological examination on full-size films (15" x 12" or 17" x 14") was extended to include a comparison of the physical measurements and the maximum voluntary ventilation (MVV) of the 2 racial groups. The methods and measurements are described in detail. Great care was taken to ensure that technically excellent films under identical conditions were made in the 2 groups.

No factors were found by which the observers could differentiate between the lung fields of the 2 racial groups. The chest configuration, as measured by the ratio vertical diameter (VD): broad diameter (BD) was almost identical in the 2 racial groups. The African, it was proved, has a significantly smaller and more compact physique than the European. The heart of the African as measured by the transverse diameter was found to be slightly greater than that of the European and the cardio-pulmonary ratio was significantly larger. The MVV of the African was significantly less than the European, but when expressed in relation to square metre of body surface area the differences were less pronounced and in the older age-groups were no longer significant.

[Professor Oosthuizen—a radiologist of international repute—recognized that his original study was of a pilot nature and the conclusions tentative. The practical implications, however, were important. Now there are 2 opposing views and these must be reconciled. Different tribes of Africans may have been involved. There is urgent need for a joint investigation on agreed lines and a joint report especially as the compensation legislation, including standards for diagnosis, for pneumoconiosis in South Africa is again under review.]

A. Meiklejohn

ASHFORD, J. R., FORWELL, G. D. & ROUTLEDGE, R. **A Study of the Repeatability of Ventilatory Tests, Anthropometric Measurements, and Answers to a Respiratory Symptoms Questionnaire in Working Coal-Miners.** *Brit. J. Indust. Med.* 1960, Apr., v. 17, No. 2, 114–21, 2 figs. [18 refs.]

[In long-term research projects such as the Pneumoconiosis Field Research of the National Coal Board [this *Bulletin*, 1959, v. 34, 1129] it is essential that measurements should be consistent—that is they should be repeatable at intervals of time and by different observers in varying circumstances. The medical and scientific teams of the Pneumoconiosis Field Research and the Pneumoconiosis Research Unit at Cardiff have continuously examined the validity of their methods and results. Indeed they have almost developed a new field of research epitomized in the term "observer error".]

This study made in working coalminers is concerned with the repeatability of ventilatory tests, anthropometric measurements and the answers to a questionary on respiratory symptoms.

Forced vital capacity (FVC) is the total volume of air which can be expired after a maximal inspiration. The forced expiratory volume (FEV) is the fraction of FVC expired at the beginning of expiration and is usually timed after 0·25 to 0·75 second or 1 second. Recommendations have been made for a standard terminology and notation [this *Bulletin*, 1958, v. 33, 355].

The use of $FEV_{1\cdot0}$ as an index of breathlessness is well established, but the use of FVC in the assessment of lung function is disputed. One of the main criticisms of the use of FVC is that the measurement may not be as reproducible as the $FEV_{1\cdot0}$.

In preparation for routine surveys at collieries throughout Great Britain a pilot survey occupying 2 weeks was carried out at 2 collieries, 1 in Fife (Scotland) and 1 at a colliery in South Wales. At each colliery the working population was divided into 5 arbitrary age classes "(under 30 years, 31–40, 41–50, 51–60 and 60 and over)." [These errors in age-grouping are all too common in scientific literature; it should be under 31 and 61 and over. In point of fact according to Table 1 the age-groups were under 30, 30–39, 40–49, 50–59, 60 and over.] 5 occupational classes, of which 2 covered faceworkers, 2 covered non-faceworkers underground, and 1 covered surface workers, were separated. Each of these 25 groups—by age and occupation—was further subdivided into 3 subgroups, in terms of shifts worked (days, afternoons or nights) on the first of the two weeks during which the trial was carried out. The subjects for examination were then chosen at random, 1 from each of the 75 subgroups. This means that 75 men were examined at colliery A (Fife) and 75 at colliery B (South Wales). 6 replicate readings of FEV [it appears from the paper abstracted below that the time was 1 second, $FEV_{1\cdot0}$] and FVC (in litres) were made by using a Gaensler type of spirometer with an electronic timing device. At both collieries separate measurements were made by 2 observers of weight, standing height and sitting height. Respiratory symptoms were recorded on a questionary, which was asked of each man on both weeks of the trial, by a doctor and 1 by a clerk.

At the Scottish colliery (A) the $FEV_{1\cdot0}$ was only slightly less variable than the FVC but at the Welsh colliery (B) the $FEV_{1\cdot0}$ was more reproducible than the FVC. While variation, both $FEV_{1\cdot0}$ and FVC, from day to day at the Scottish colliery was small, that at the Welsh colliery was the more variable of the 2 measurements. The authors comment on these findings thus: "The absolute value of the F.V.C. measurements was, of course, greater than that of F.E.V., and if this fact is taken into account, it is apparent that the proportional variation of F.V.C. was very little different and if anything slightly smaller than that of the F.E.V."

As to measurements of weight and height, the differences between observers were negligible. In general the answers to questions on respiratory symptoms obtained by doctor and clerk were in close agreement.

[The next abstract is a sequel to the foregoing and the two should be read in conjunction]. *A. Meiklejohn*

DUFFIELD, D. P. & ASHFORD, J. R. **A Study of th Reproducibility of the Forced Vital Capacity c Coalworkers at Two Collieries in Scotland an Two Collieries in South Wales.** *Brit. J. Indus Med.* 1960, Apr., v. 17, No. 2, 122–4.

Routine physiological surveys of FVC and FEV_1 were made at colliery C in Ayrshire, Scotland, and colliery D in South Wales. These followed the pilo surveys at collieries A and B [see preceding abstract The number of men—practically the entire population—at colliery C was 853 and at colliery D, 519. [Thes with 75 men at A and 75 men at B account for the figur 1522 mentioned in the text.]

The apparatus used in this study was the modifie spirometer described by MCKERROW *et al.* (1960, *Lance* v. 1, 149), altered to permit direct readings of FVC an $FEV_{1\cdot0}$.

On the basis of the combined observations in the pilo and routine studies the authors conclude that the FV was as reproducible a measurement as the $FEV_{1\cdot0}$, an that the reproducibility was virtually unaffected by th presence or absence of bronchitic symptoms or the diffe ent prevalence of pneumoconiosis at collieries C and D

[The National Coal Board are to be commended fo permitting interim publication of the work of teams i the Pneumoconiosis Field Research. On this occasion however, some confusion to readers and repetition migh have been avoided if the pilot and routine studies ha been combined in a single paper. In the desirable aim of standardization of methods and presentation of resul readers would have expected that in these papers th authors would have followed the recommended notatio of FEV.] *A. Meiklejohn*

BECKLAKE, Margaret R., ZWI, S. & LUTZ, W. **Studie on the Nature and Aetiology of Respiratory Dis ability in Witwatersrand Gold-Miners free o Radiological Silicosis.** *Brit. J. Indust. Med.* 195 Oct., v. 16, No. 4, 290–96, 1 fig. [20 refs.]

In recent years doctors investigating the lung disease of miners—particularly in goldmines and coalmines—have been concerned to explain pulmonary disability i the absence of specific radiological evidence of pneumo coniosis [this *Bulletin*, 1956, v. 31, 1234].

There appear to be three possible causes of disabilit (or any combination of these) in such cases:

(1) Psychogenic factors producing exaggeration o symptoms (including malingering);
(2) Presence of other lung disease (*e.g.*) bronchiti bronchospasm or emphysema;
(3) Presence of dust fibrosis as yet radiologically unde tectable.

A random sample of 45 goldminers was selected fro 314 men attending the Pneumoconiosis Bureau at Johan nesburg between December 1955 and May 1956. Th men were in the age-group 41–45 years and in each cas 3 readers were agreed that the radiological appearance were normal (cases with increased lung markings wer excluded). 34 of these were finally tested but for reason stated the loss of 11 was held not to bias the sample

The risk was restricted to rock-breaking service in goldmines and was measured in particle hours (hours of underground service × average konimeter count in scheduled mines at relevant years of service). The smoking habits of each man were ascertained and dyspnoea was graded on the scale suggested by FLETCHER [this *Bulletin*, 1953, v. 28, 121]. Each case was investigated clinically. Measurements of lung volume, maximum voluntary ventilation (MVV), compliance, and non-elastic resistance were made with the subject seated. Lung volume subdivision, MVV, and the ventilation volumes were expressed at BTPS [body temperature and pressure saturated with water vapour]. Age was recorded to the nearest year, height with the subject in socks, weight with light clothing. The findings are tabulated in detail. No significant relationship was found between dyspnoea and dust exposure or smoking. However, a negative correlation was observed between dust exposure and effort tests, implying that exercise capacity appeared best in those men whose dust exposure was greatest [these men may have initially been above average]. Dyspnoea correlated with airway obstruction and hyper-ventilation, indicating a physiological rather than a psychological basis for the symptom. The higher incidence of cough, sputum and rhonchi in the more disabled subjects suggested that chronic bronchitis might be the basis of their symptoms but the cause of the bronchitis remains to be identified. It seems that dust exposure alone was not the cause, but the findings do not exclude the possibility of its being related to the occupation of mining with stresses such as inhalation of fumes and rapid changes in temperature, humidity and altitude.

The authors emphasize that:

"It is important also to stress that in studies in which dust exposure is assessed retrospectively over many years, the inherent inaccuracies place a severe limit on the validity of the conclusions. To provide a clear-cut answer to the effect of dust exposure on pulmonary function, prospective studies are required in which dust exposure is accurately recorded and pulmonary function is assessed at regular time intervals."

[This indeed is the approach of the Pneumoconiosis Field Research (25 pits scheme) which is currently being carried out by the National Coal Board in Great Britain.] *A. Meiklejohn*

MOTLEY, H. L. **Pulmonary Function Impairment in Pneumoconioses.** *J. Amer. Med. Ass.* 1960, Apr. 9, v. 172, No. 15, 1591–5, 2 figs. [12 refs.]

This is a study of 98 diatomaceous earth workers who are still at work and have no major complaints. Heating crude diatomaceous earth changes amorphous silicon dioxide to crystalline crystobalite. Exposure to this dust results in silicosis and can produce marked pulmonary insufficiency in less than 5 years [this *Bulletin*, 1953, v. 28, 351]. Of the 98 cases, 41 showed no radiographic changes, 33 had linear nodulation, and 24 nodular confluent appearances. Pulmonary function was impaired in 68 cases, 6 of these to a severe degree. But there was an overall lack of co-ordination between the degree of pulmonary function impairment and the radiological findings. Single tests of lung function or only of one aspect are unsatisfactory. So what is described as a battery of tests was used to determine the ventilatory state, the transport of oxygen and carbon dioxide in the lungs, and the pulmonary blood flow. The interpretation of the results of those tests is discussed.

In addition the results of these tests are tabulated in 3 other cases, one a worker in diatomaceous earth, one in hard coal, and the third in asbestos. The cause of the impairment was poorly ventilated alveoli or a perfusion of blood through non-ventilated areas. It is asserted that the presence of an alveolar capillary membrane block has not been found to be a significant factor in pneumoconiosis. Even in interstitial pulmonary fibrosis and other restrictive conditions of the lungs, hypoxia results from perfusion of blood through non-ventilated areas and not from alveolar capillary membrane block.

Charles L. Sutherland

HALMAGYI, D. F. J. **Dorsal Kyphosis in Chronic Obstructive Lung Disease.** *Lancet.* 1959, Feb. 28, 446–8, 6 figs. [20 refs.]

The relation between kyphosis, lung disease, ventilatory capacity and age were investigated in 360 miners admitted to hospital for respiratory complaints—pneumoconiosis, primary obstructive emphysema or bronchial carcinoma (300)—or conditions other than chest disease (control group of 60).

Kyphosis was assessed by the angle on lateral chest X-ray film between the tangents of the anterior borders of the 2nd and 11th thoracic intervertebral spaces (kyphotic angle). Disease of the spine was noted. Ventilatory capacity was measured by indirect maximal breathing capacity method (MBC). Pulmonary hypertension was diagnosed by electrocardiograms.

The kyphotic angle increased 0·22° per year in controls: in respiratory disease the overall degree of kyphosis and the increase per year (0·68°) were greater.

The maximum breathing capacity diminished by 1 litre per minute for every 0·138° increase in kyphotic angle.

Electrocardiographic results indicated that pulmonary hypertension was related to severity of lung disease (assessed by MBC) but was not unduly prevalent in patients with kyphosis. *M. L. Thomson*

SMITH, R. A. **Lung Cancer in Coal-Miners.** *Brit. J. Indust. Med.* 1959, Oct., v. 16, No. 4, 318–23, 9 figs.

Cancer of the lung presenting radiographically as a single massive shadow may supervene in a miner suffering from pneumoconiosis. In this situation the differential diagnosis from the more common condition, complicated pneumoconiosis or progressive massive fibrosis (PMF) is sometimes difficult and mis-diagnosis is not uncommon [this *Bulletin*, 1960, v. 35, 20]. In the present paper this is illustrated in 5 case-histories.

Follow-up of 320 patients—non-miners—operated on for bronchial carcinoma at the Thoracic Surgical Unit, King Edward VII Memorial Chest Hospital, Warwick,

England, showed that only 36% survived 2 years or more. This accords generally with experience elsewhere. During the same period and with the same criteria of operability, 21 coalminers were treated by resection and of these only 3 (14%) died in the first 2 years; this represents a survival rate of 86%, which is interpreted as signifying that a coalminer has an appreciably greater chance of survival than a non-miner. The two most likely explanations of these results are that the rate of local growth and spread of the tumour are considerably retarded by the effects of prolonged inhalation of coal-dust on the lung parenchyma and lymphatics, or that the coalminer develops a specific and slow-growing type of tumour. James [this *Bulletin*, 1955, v. 30, 766] found no evidence to support the second explanation from microscopic examination of a large number of lung tumours in coalminers. The former explanation is considered to be the more attractive and the author submits that the favourable post-operative results in coalminers merits further consideration.

[A more detailed presentation of the facts would have assisted in an assessment of the validity of the hypothesis and in guidance for future observers. The beneficial effects of a little coal-dust are increasing:— protection against tuberculosis infection, improved pulmonary ventilation and prolonged survival in cancer of the lung.]

A. Meiklejohn

Anderson, W. H. & Schmidt, W. F. **Evaluation of Disability in Coal Miners with Chronic Pulmonary Disease.** *J. Amer. Med. Ass.* 1959, Sept. 12, v. 171, No. 2, 145–50, 3 figs. [11 refs.]

Disability was evaluated in 482 subjects, mainly miners, by 3 pulmonary function tests, (1) maximum breathing capacity (MBC), (2) vital capacity (VC), and (3) timed vital capacity (TVC). The results of these tests were correlated against clinical breathlessness graded in 7 categories (1) hard work, asymptomatic, (2) hard work, shortness of breath (SOB), (3) sedentary work, asymptomatic, (4) sedentary work but complains of SOB, (5) unable to work because of SOB, (6) retired, asymptomatic, (7) retired, SOB.

All tests showed a correlation with clinical grade but the MBC showed the highest correlation and discriminated best between normal and disease. This reinforces the conclusion of Gilson and his colleagues [this *Bulletin*, 1956, v. 31, 825] in their study of Welsh coalminers and of Motley *et al.* [*ibid.*, 1950, v. 25, 277] in miners with anthrasilicosis.

If MBC is 60% of normal or less in a person complaining of SOB he is most likely disabled for hard work: above 60%, arterial oxygen studies should be performed to exclude arterial anoxaemia. When this has been done about 13% of persons remain who allege inability to work because of SOB; some of these are neurotic.

M. L. Thomson

Watson, A. J., Black, J., Doig, A. T. & Nagelschmidt, G. **Pneumoconiosis in Carbon Electrode Makers.** *Brit. J. Indust. Med.* 1959, Oct., v. 16, No. 4, 274–85, 11 figs. [16 refs.]

The aetiology of progressive massive fibrosis (PMF otherwise complicated pneumoconiosis, is unsolve Several hypotheses have been advanced to explain development. European pathologists, notably Di Bia (Germany) [this *Bulletin*, 1951, v. 26, 786] believe th the confluence and collagenization of coal-dust macul is somehow due to the action of silica contained in ther In Great Britain the majority of observers including th Pneumoconiosis Research Unit, Cardiff, support th view that the fibrotic masses represent tuberculous lesio modified by the presence of coal-dust [*ibid.*, 1948, v. 2 414; 1952, v. 27, 169; 1954, v. 29, 962]. Doig, one the authors of the present paper, is of opinion that major factor in the production of massive fibrosis in coa workers is the occurrence of atelectasis of the alveo between discrete lesions, thereby forming a dense, airle mass which, owing to changes in the vessel walls, is i supplied with blood in which infection and necros readily occur.

Recent experience of pneumoconiosis in carbon ele trode workers would seem to add to understanding of th problem or at least to direct attention to a potential fruitful field of future study. In the production aluminium in electric furnaces large block carbon ele trodes are used. These blocks are made in a speci department in the works. Coke and anthracite—special selected for low mineral content—are ground, mixed wit a binder, usually pitch, and pressed into the require shapes. Until 1945 at the factory investigated the oper tions were extremely dusty but since then measures ha been successful in minimizing the dust clouds. In 194 Doig examined 15 workmen employed in the processe The duration of their employment at risk was betwee $10\frac{1}{2}$ and 39 years. 9 cases of pneumoconiosis were diag nosed, 5 simple and 4 complicated (PMF). One case simple pneumoconiosis was observed after 13 years an one of complicated pneumoconiosis after 18 years. Th detailed findings of the 15 cases are tabulated. Case 15, man aged 61 years, who developed complicated pneum coniosis after 19 years, died and his lungs were examine at necropsy. Two additional cases (Nos. 16 and 17 carbon electrode workers at the same factory but wh were not included in the survey, were also examined necropsy. The paper includes a detailed account of th pathology, histology and bacteriology of these 3 case 1 simple pneumoconiosis and 2 complicated pneum coniosis and is illustrated by radiographs, Gough sectio and histological sections [the *British Journal of Industri Medicine* merits commendation for the excellence an completeness of the illustrations].

Analysis of the lung dust in the 2 cases of complicate pneumoconiosis (PMF) was made according to th method of King *et al.* [this *Bulletin*, 1956, v. 31, 641 The mineral residues were examined by X-ray diffractio and partial chemical analysis. The amounts of carbona ceous matter (coal and coke) found in the lungs wer considerable. The most significant finding was th quartz—silica—was almost completely absent. Virulen tubercle bacilli occurred in case 16. The authors subm that the findings are incompatible with the "silica hypothesis of causation of progressive massive fibros and provide some limited support for the "tuberculosis hypothesis.

[This is a very important contribution. It does not solve the problem but it focuses attention on a group of workmen among whom cases of progressive massive fibrosis may occur in the future. Indeed workmen in many industries are exposed to the inhalation of carbon black, "nearly pure carbon". It is hoped that doctors will be alert to the occurrence of pneumoconiosis among such workers and assure the fullest possible investigation of every case.] *A. Meiklejohn*

BEITRÄGE Z. SILIKOSE-FORSCHUNG. [1960], 385 pp., numerous figs. [Numerous refs.] Grundfragen aus der Silikoseforschung. Dritter Band. Bericht über die von der Bergbau-Berufsgenossenschaft am 5. und 6. Dezember 1958 in Bochum veranstaltete Tagung der Arbeitsgemeinschaft für Silikose-Grundlagenforschung. **[Fundamental Silicosis Research, Volume 3; Report of a Conference in Bochum, December 1958]**

The pneumoconiosis insurance authority of the Mining Industry in Western Germany (Bergbau-Berufsgenossenschaft) arranges annual conferences of research workers to discuss progress in fundamental silicosis research. The present report (volume 3) gives the papers and discussions of the last of these conferences, held in Bochum in December 1958. In a valuable introduction the editors point to 4 fields in which important work is going on now and mention a fifth which may become important in the future. These are:

1. The quantitative study of dust elimination from the lungs of animals and a study of the size distribution of lung dust by optical and electron microscopy [subjects which were more recently discussed at the International Symposium on Inhaled Particles and Vapours in Oxford, April 1960].
2. The study of surface activity versus solubility of silica, where interest has now shifted to the processes occurring inside phagocytic cells.
3. The study of the interaction of dust and cells by biochemical and electron microscope techniques.
4. The study of immunological reactions in silicosis.
5. The metabolic activity of the lung apart from its function for gas exchange.

The Conference was arranged in 5 sessions. The first dealt with lung dust, the second was labelled morphological investigations, the third and fourth were devoted to immunological reactions and the last dealt with miscellaneous items. This order will be followed in the present review.

Part A, *Lung Dusts* opens with a paper by H. OTTO (pp. 17–20) which dealt with lung dust analyses from the ceramic industry, a term which includes the manufacture of silica brick, pottery, porcelain and refractories, and talc (steatite). The total and incombustible dust was determined as grammes per lung by the formamide method and the acid-insoluble ash was examined by phase contrast microscopy and X-ray diffraction. When the lungs were arranged in increasing amounts of incombustible dust this order corresponded to the pathological classification, 2–3 gm. of mineral dust for slight silicosis, 3–4 gm. for medium, and between 4 and 33 gm. of minerals for advanced silicosis with massive lesions. On an average 60–70% of the total lung dust was incombustible.

A paper by A. WEISS, G. HOFMANN and G. REIFF from Darmstadt (pp. 21–34) points to discrepancies between chemical and mineralogical analyses of lung dust isolated by the formamide method. The total silica was always in excess of the silica which could be ascribed to quartz, mica, kaolin and felspar, and it is therefore assumed to be amorphous silica. In contrast to the proportions of total silica or quartz, the amount of this amorphous silica was related to the degree of silicosis; it increased on an average from 2% of the lung dust for silicosis grade I to 7% for grade III. A technique based on esterification with pyrocatechol was developed to demonstrate the presence of amorphous silica together with quartz and silicates, and when applied to a few lung dusts it gave good agreement with the calculated amounts. The author appears to believe that this amorphous silica is liberated by the formamide treatment from water-insoluble organic silicic acid esters present in the lungs. These esters may occur in proportion to the amount (and length of time) of quartz surface present in the lung [nothing was said about their possible aetiological significance].

In another contribution by Weiss from the same Institute (pp. 45–65) the universal occurrence of a mica-like mineral in silicotic lung samples is deduced from X-ray diffraction observations. This material gives a poor mica pattern with a slightly larger basal spacing, d = 10·3–10·5 Å, than other known mica minerals. By ion exchange with dodecylammonium ions the spacing could be enlarged to 35 Å and under similar conditions muscovite and illite gave spacings of about 40 Å. A number of catalytic reactions given by various substances introduced between the layers of silicates of the mica type are described in order to explain the possible significance of this new observation. At the proof stage the authors add that this type of mica-like material is also found in the lungs of rats 5 months after inhalation of pure quartz dust.

Animal experiments with raw and calcined talc are described in the following paper by H. LÜCHTRATH (pp. 69–76). The technique was intratracheal injection into rats, with observations lasting up to 20 months after injection. Raw talc was found to be inert but calcined talc which contained 10% of cristobalite and quartz was fairly fibrogenic. The author points out that inferior grades of asbestos are often mixed with talc or even sold as "talc" and that lung fibroses ascribed to talc may well be caused by quartz or asbestos mixed with such talc.

The last paper in this group by E. SCHILLER (pp. 77–84) dealt with tests on rats of a series of dusts which are intermediates or finished products of the cutting tool industry. Metal, carbide, and oxides of tungsten, tantalum and titanium were found to be inert. Cobalt metal injected into the trachea at 1 mgm. per rat gave an acute inflammatory reaction with lung oedema; however, 2 months later the lungs were normal. The author concludes that it would be premature to legislate for lung fibroses due to inhalation of dust in the hard metal industry. The paper is illustrated by excellent coloured microphotographs of tissue sections.

Part B, *Morphology*, begins with an electron microscope study of mature silicotic lesions from rats' lungs by H. W. Schlipköter and E. Lindner (pp. 93–101). The paper is mainly descriptive. This is followed by a similar study of fibre formation in a human embryo by W. Schwarz and H. J. Merker (pp. 103–115), and a study of fat absorption in rats' lungs which showed that inhaled fat was stored or eliminated, and fat ingestion did not lead to any increase in the lipid content of the lung tissue (A. Kluge, pp. 119–126).

Next come two important papers on dust clearance. Rats were exposed to quartz dust clouds defined by size and concentration, and the dust elimination was followed over periods of 1–9 months.

In the first paper by K. D. Friedberg and H. Polley (pp. 129–144) quartz dust loads below 1 mgm. per lung gave retention values after one month of the order of 32–36%; with dust loads between 1 and 3 mgm. retention after one month rose to 50–70% of the value found 10 hours after the end of dusting (Table 1). Detailed analyses of different lobes up to 6 months after dust inhalation showed slightly better dust clearance for the lower than for the upper right lobe.

In further studies they tried to modify the dust elimination. Keeping the rats cold at 4–9°C. increased retention slightly while keeping them at 32°C. had no effect. Aerosol, exercise after inhalation, and various drugs also had no effect. Subcutaneous injection of colloidal dyes such as Evans Blue slightly reduced the elimination rate and when the rats were made to inhale graphite for 3 days before the quartz inhalation there was no quartz elimination at all after 30 days. Guineapigs had a higher retention capacity than rats.

In the second paper, by W. Klosterkötter and G. Bünemann (pp. 145–157) similar experiments with quartz and other materials are described but the rates of elimination of quartz were in general much lower (Table 1).

TABLE 1

SiO_2 retained as per cent. of amount found after one day
Data obtained from two laboratories

Initial dose of quartz mg/rat	After 1 month		After 3 months		After 5 or 6 months	
	Lab 1	Lab 2	Lab 1	Lab 2	Lab 1	Lab 2
0·1	34					
0·2		62				
0·3	32					
0·4	34	78	9	55		
0·7	36			67		57
1·7	53					
2·6		88				72
3·0	84		53		29	
5·4		88		67		

No explanation of this discrepancy was given in the subsequent discussion. [The dust generators were different. In paper 1 the dust was freshly produced by abrasion of sandstone, in paper 2 à previously ground dust was dispersed. The state of aggregation of the particles may have been different.] Various other results reported in the second paper are given by the authors elsewhere [this *Bulletin*, 1960, v. 35, 642].

Parts C and D dealt with the *Immunological theory* o *silicosis*, which is studied in many laboratories at th present time. E. Vigliani (pp. 165–177), B. Pernis (p 179–191) and G. Mottura and F. Levis (pp. 193–20 reviewed the subject and presented new experiment evidence in favour of it. Briefly they see the first ste in silicosis in the death or inactivation of the phagocyt cells which ingest quartz or other forms of free silic (etched quartz and tridymite are the most active of these The detailed mechanism of this process is as yet un known. The dead cells seem to have two effects: (a) the attract fibroblasts which leads to the laying down of ret culin and later collagen fibrils, (b) they stimulate th reticulo-endothelial system (plasma cells are attracted and a mixture of beta and gamma globulins is precip tated around the fibres. This leads to the formation o the silicotic nodule. Its protein (hyaline) contains ca.40% collagen and 60% globulins. Apart from these there ar per 100 parts of protein, about 15 parts of lipids and parts of polysaccharides.

Vigliani summarized various observations which sug gested that this precipitation of globulins on the collage was an immunological reaction but he carefully adde that they did not amount to a definite proof of th hypothesis. Pernis gave further experimental evidence o the fact that silica acted like a kind of permanen Freund adjuvant (increased resistance towards infection in mice, and increased bactericidal power of serum o rabbits after injection with tridymite, and increase i formation of anti-ovalbumin antibodies in rabbits); h concluded by saying that silicosis belonged to the field o non-specific immunity and that there probably was n specific antigen. Earlier it had been thought that quart with adsorbed protein, or lipopolysaccharides liberate from the attacked macrophages were perhaps suc specific antigens.

Mottura dealt chiefly with the histological evidenc After injection or inhalation of quartz there is first th formation of deposits of often severely damaged macro phages. This is followed by histiocyte accumulation an by slow emergence and then finally accumulation o plasma cells; there is also a fluctuating amount of pyro ninophilic immature cells around the lesions. In the dis cussion it was considered possible that auto-endotoxin could be liberated from the macrophages inactivated b quartz, and it might be possible to demonstrate this b further experiments.

Several papers dealt with quartz-serum agglutinatio experiments of the type first described by Scheel *et a* [*ibid.*, 1954, v. 29, 634]. The effects were found to be du to contamination with dead bacteria in one laborator (Schlipköter, pp. 241–246) but in another this was dis proved (H. Antweiler and E. Hirsch, pp. 247–249 while a third (Klosterkötter, pp. 255–263) did not obtai conclusive evidence either way. Doubt was thrown o the validity of observations of coagulation of quart suspensions which may depend on such external factor as standing in an ice-box overnight, or on other detai of technique rather than on antigen-antibody precipita tion. H. Lüchtrath (pp. 251–253) showed that no sensitiza tion occurred when intraperitoneal injections of quart were made in rats 4 months after they had receive quartz by intratracheal injection.

Part E of the book contains a rather miscellaneous collection of papers, among them an electron microscope study by K. KRISCH, H. W. SCHLIPKÖTER, H. STAUDINJER and J. LEHMANN (pp. 279–287) of the swelling of isolated liver cell mitochondria in water and in monosilicic acid, and further experiments on epitaxy of amino acids and polypeptides on quartz by H. SEIFERT (pp. 291–300), both in aid of theories which have been abandoned by most workers in this field. There is also a study by H. HÖRMANN and T. L. NAGABHUSHAN (pp. 301–306) of the effect of finely ground quartz on trypsin, which shows a little adsorption without inactivation of the enzyme, and a study of polysilicic acid interaction with serum proteins by K. D. FRIEDBERG and H. J. HILDEBRANDT (pp. 307–312) who found that the bonding between them is reversible, as all silica could be removed by dialysis, leaving behind a permanently denatured protein with a higher proportion of gamma globulins than had been present in the original serum. *G. Nagelschmidt*

CHVAPIL, M. Möglichkeiten einer quantitativen Bestimmung des Fibrosegrades bei der Untersuchung experimenteller Silikose. [**Possibility of determining Quantitatively the Degree of Fibrosis in Experimental Silicosis Studies**] *Beiträge z. Silikose-Forschung.* 1960, No. 64, 71 pp., 12 figs. [Numerous refs.]

In an introductory review, the need for, and difficulties of, quantitative determinations of fibrosis are discussed. There are several different types of collagen and reticulin, some of them soluble in salt solutions and alkalis.

The author has chiefly used the following methods:

For analysis of lungs he adds stannous chloride equal to half the dry weight of the sample and hydrolyses the mixture with 6N HCl for 4 hours at 5 atmospheres. After neutralizing, the precipitate of stannous hydroxide is washed repeatedly with hot water to remove adsorbed hydroxyproline, and the latter is determined by Stegemann's modification of the Neumann-Logan method. Tyrosine may cause a maximum error of 2·5% in this method but no correction for tyrosine is necessary if comparisons are made between controls and experimental animals.

For analysis of liver tissues he extracts collagen with trichloroacetic acid according to FITCH *et al.*. (*Nature*, 1955, v. 176, 163) before the hydrolysis and hydroxyproline determinations. Another technique which the author used is gravimetric determination of total "scleroprotein" (after dissolution of soluble proteins and lipids according to LOWRY *et al., J. Biol. Chem.*, 1941, v. 139, 795).

In certain cases the author prefers to give hydroxyproline rather than "collagen" values because a part of hydroxyproline may be present in soluble forms of collagen.

The author has studied the effect of age (or weight) on collagen and hydroxyproline content of the lungs and livers of rats and mice, and the results are given in tables and figures. After about 2 months, the collagen content of the livers of both species had reached a fixed value of the order of 1–2% of the dry weight of the organ and remained constant. The collagen content of the lungs, however, continued to rise with increasing weight of the animals. This rise goes from about 5 to 10% dried lung for mouse lungs when the weight of the animal ranged from 5 to 35 gm. and from 10 to 15% dried lung for rats between 100 and 400 gm. Part of the increase in rats may be due to fibrosis following infections. The dry weight, as percentage of wet weight, increases with age from about 19% for rats weighing 100 gm. to 21% for rats weighing 350 gm.

There is a long discussion of these results. They are said to follow a parabolic law: $Y = aX^b$, where Y is the weight of the organ, X the weight of collagen or hydroxyproline, and a and b are constants. If the logarithms of X and Y are plotted, this leads to straight lines with slope b, and values for "b" from the present work are listed and compared with other data from the literature.

A table (No. 10) is given which shows that in 12 rats of 18 months age the coefficient of variation of the total amount of hydroxyproline per lung was 17% as compared with 22% for dry or wet weights of the lungs. The mean weight of the rats was 397 gm., and the mean dry weight of the lungs was 741 mgm. and the mean total hydroxyproline was 7·45 mgm.

[On the conventional value of 13·4% hydroxyproline in collagen, this would give an average collagen content of 7·5% for the lungs, which is only about half the value given earlier in Table 4 and Fig. 1 for "scleroproteins" of rats of about that weight.]

In the second part of the paper the use of hydroxyproline determinations in experimental silicosis is described.

Four different methods are mentioned: (1) Intratracheal injection into rats and analysis of the lungs. (2) Intravenous injection into mice or rats and analysis of livers. (3) Injection into the lymph sac of frogs and analysis of the spleen. (4) Effect of dust on chicken embryo tissue cultures.

The frog tests were preliminary and showed that quartz increased the weight of the spleen, and the total hydroxyproline in it, significantly over that of controls injected with saline.

The tissue culture tests were carried out 4 and 8 days after adding dust to 15-day-old cultures. They showed that quartz depressed but polysilicic acid in certain conditions stimulated collagen production (*Brit. J. Indust. Med.*, 1959, v. 16, 286).

The author had no experience with intraperitoneal injection and liver analysis but believes this to be a good method; most results in this part deal with intratracheal injection of 50 mgm. of quartz of 1·5 micron mean size into rats. A number of graphs show that 2 to 6 months after injection the lung weights were not significantly different from those of the controls although their water content tended to be higher. [The amount of hydroxyproline produced 6 months after injection was surprisingly small and exceeded that of the controls by less than 50%. It is very difficult to make a direct comparison with the controls from the data given in the paper which seems to be a review of several papers published elsewhere.]

The point is made that the weight of the organ may vary through changes in diet, vitamin doses, etc., and the

hydroxyproline as per cent. of the lung weight may therefore give misleading information. The absolute values of lung weight and hydroxyproline should both be examined.

A detailed study of the different collagen fractions showed that alkali-soluble collagen rises to a peak during the first month and may amount to one-third of the total collagen; its proportion then decreases again and remains constant from 4 to 6 months. This may lead to the possibility of shortening the period of observation after intratracheal injection.

After discussing various other papers and different ways of expressing the results of the measurements, such as correcting for body weight, the author concludes that the best method for assessing fibrosis is to give the absolute amounts of collagen per lung.

This is a valuable paper in which much detailed information is given. The author rightly stresses the importance of biological variability and the need for statistical assessment of the data obtained.

G. Nagelschmidt

CHARBONNIER, J., COLLET, A., LE BOUFFANT, L., DANIEL-MOUSSARD, H. & DURIF, S. Die Beziehungen zwischen Struktur, Löslichkeit und Gewebetoxizität der verschiedenen Minerale. [**The Connexions between Structure, Solubility and Toxicity to Tissues of Various Minerals**] *Beiträge z. Silikose-Forschung.* 1960, No. 66, 3–31, 17 figs.

This contribution on the pathogenesis of silicosis consists of two experiments. The first is a study of the effects of minerals of different crystalline structure when injected intraperitoneally into rats. Two theories have been put forward to explain the fibrogenic action of minerals. The solubility theory rests on a specific effect of dissolved silica; the physical theory assumes that protein is adsorbed on the crystal surface, so that substances with the same crystalline structure should produce similar damage. Quartz and cristobalite both produce fibrosis, and the authors study the question of whether this is true of other chemical substances which have the same crystal structure as quartz and cristobalite. Contradictory results have been obtained by various workers, for instance STACY *et al.* [this *Bulletin*, 1959, v. 34, 907] and MARKS *et al.* [*Ibid.*, 1957, v. 32, 47].

4 substances were investigated: quartz, aluminium phosphate with a quartz type of crystal structure (hexagonal), cristobalite, and a cristobalite type (tetragonal) of aluminium phosphate. Each was reduced to a powder of particle size under 3 microns, and checked in various ways, in particular as regards solubility and X-ray diffraction pattern (X-ray diagrams are shown). Each rat received 100 mgm. of one of the dusts in isotonic salt solution intraperitoneally. At the end of 31 days the lesions were investigated, the naked eye appearance and collagen content were noted and histological examinations made. The illustrations of the histology show clearly the differences in the effects of these dusts. The cristobalite reaction was greater than that of the quartz; both were markedly fibrogenic in action. On the other hand, the phosphates produced practically the same minimal reaction. They acted as inert dusts giving ri to a slight cell destruction and a small amount of fibr sis. It is therefore concluded that the chemical natu of the dust is of greater importance; the crystal structu has an effect only if the dust is actively fibrogenic.

The second experiment was designed to answer t question: if, to be dangerous, a dust must show a certa solubility, how will an insoluble silica behave? A ne form of silica (monoclinic system) was compared in effect with quartz, using rats in the same way and maki examinations after 4 and 21 days. Owing to the har ness of this silica it could not all be reduced to a partic size under 3 microns; the quartz was therefore reduc to a comparable size. The reaction to the quartz w quite definitely a fibrosis, while the insoluble silica pr duced only the slight fibrotic reaction of an inert du To meet the objection that this result might be due the difference in crystal structure it is pointed out th non-crystalline forms of silica can produce fibrosis. is submitted that the behaviour of this insoluble sili contributes an argument in favour of the solubili theory. *Charles L. Sutherland*

GIULIANI, G. **Radiological Features of Pulmonar Silicosis in the Guinea Pig.** *Scientia Med. Italic* 1959, Oct.–Dec., v. 8, No. 2, 175–91, 5 figs. [2 refs.]

Guineapigs were exposed to the inhalation of amo phous silica under conditions practically similar to tho in silicosis-producing industries. Details are given of t dusting chamber in which the animals were exposed the dust for 5 to 7 hours daily for 5 days a week. posterolateral and a lateral X-ray film of the chest w made before exposure and every 30 days thereafte After 10 to 14 months a diffuse increase of density w observed spreading from the hilus. As time went this density increased and spread to the periphery. the end of 18 to 26 months the density was so great th the cardiac shadow was obscured. There was no vari tion in different parts of the lung and no nodulatio Dyspnoea was very slight at first but this increased t death supervened. Pathological examination of t lungs showed no nodulation. There was a general fibr sis with a maximum concentration at the hilar regi which lessened towards the periphery. Histology co firmed this. The alveolar walls were congested at fi with desquamated cells in the lumen. Later the alveol walls became thickened and the lumen diminished. N silicotic nodules were demonstrable.

It is concluded that the lesions produced by silica the lungs of a guineapig are different from those pr duced in the human lung. *Charles L. Sutherland*

SCHLIPKÖTER, H. W. & BROCKHAUS, A. Die Wirkun von Polyvinylpyridin auf die experimentelle Silikos [**The Effect of Polyvinylpyridine on Experimenta Silicosis**] *Deut. med. Woch.* 1960, May 20, v. 8 No. 21, 920–23, 933–4, 955, 10 figs. (8 on 2 pls.)

If monosilicic acid causes silicosis, as assumed by th silica solubility theory, then in order to prevent silicos

the silicic acid could perhaps be removed by anion exchange. Solid anion exchangers are undesirable because they increase the dust load of the lung, but water-soluble anion exchangers might be tried. On this idea the authors made a number of samples of polyvinyl pyridine by controlled polymerization of 2- and 4-vinyl pyridine (P-2VP) and (P-4VP) and removed the remaining monomer by steam distillation. Studies showed that at *p*H 2 to 4 some adsorption on quartz took place.

The paper describes the results of animal experiments. 50 mgm. of quartz were suspended either in water or in 1% PVP solution and injected into rats intratracheally, with observations lasting up to one year, or intraperitoneally with observations up to 6 months after injection.

7 samples of P-2VP and 10 samples of P-4VP of variable degrees of polymerization were tested, each in 60 rats. There were strong and obvious differences between the quartz controls and the quartz plus PVP rats. The latter showed less increase in lung weight after intratracheal injection and had, after one year, only reached fibrosis of grade 2 (Belt and King) when the quartz controls showed grade 4 fibrosis. Similar differences were seen in the intraperitoneal tests. The lesions remained small and soft and showed only little collagen. All P-2VP samples had much the same protective effect but mortality increased with molecular weight, and P-4VP had to be used at a lower concentration because mortality was very high.

Attempts were then made to give quartz and PVP separately. When P-2VP was injected intraperitoneally 3 hours after the quartz infection its protective action was much reduced. When it was given before the quartz it acted well. Aerosol inhalation of P-2VP during 3 hours on 5 days per week after intratracheal injection of quartz also gave good protection. The mechanism of this protective action is not certain and requires further study.

G. Nagelschmidt

Posner, E. **Pneumoconiosis in Makers of Artificial Grinding Wheels, including a Case of Caplan's Syndrome.** *Brit. J. Indust. Med.* 1960, Apr., v 17, No. 2, 109–13, 3 figs. [39 refs.]

Mass miniature radiography surveys during 1953 and 1955 at a factory producing artificial grinding wheels—grindstones—revealed cases of pneumoconiosis, mostly of silicotic type. All the cases were traced to one department where the so-called "bond" is prepared and mixed with the abrasive grains of carborundum (silicon carbide) and artificial corundum (aluminium oxide). In the preparation of the ceramic vitrified bond, powdered flint—free silica—was incorporated so that it approximated to the composition of a pottery earthernware body (21% to 38% free silica).

Among 42 workmen employed in 1955 and who had not previously worked in any silica risk, 17 cases (40·5%) of pneumoconiosis—11 simple and 6 complicated—were diagnosed. No case occurred where the exposure was under 5 years, but 8 cases occurred between 5 and 15 years' employment.

Meantime 2 further surveys have been made. Only 1 new case was discovered and none of the men previously diagnosed as cases of simple pneumoconiosis had developed progressive massive fibrosis. 2 of the men died and classical silicosis with progressive massive fibrosis was observed at necropsy. 1 case showed the characteristic opacities of Caplan's syndrome. The case history is set out in detail and illustrated by radiographs.

Measures have been taken to prevent the disease; non-siliceous bonds, such as synthetic resins and rubber and frit—fused silica—are being used as substitutes for free silica.

Posner suggests that some cases of pneumoconiosis, attributed to carborundum, may be due to the binding materials for artificial grinding wheels.

[Between 1930 and 1937 the reviewer certified several cases of silicosis—confirmed post-mortem—at this factory. At that time the risk, which was of a very high order, derived from the shovelling of powdered flint and its use in kilns where the wheels were fired.

As to the occurrence of pneumoconiosis—silicosis—in users of carborundum wheels in the grinding of cutlery and edge tools, many of the cases commencing about 1928 were probably due to previous work on natural sandstone grindstones.] *A. Meiklejohn*

Hayes, D. S. & Posner, E. **A Case of Caplan's Syndrome in a Roof Tile Maker.** *Tubercle.* 1960, Apr., v. 41, No. 2, 143–5, 1 fig. [15 refs.]

The patient was a man of 50 who had been employed making roof tiles in a factory in Stoke-on-Trent. Over most of the man's exposure the tiles were hand-made from a local clay in a mould the inside of which was dusted with fine coal dust or quartz sand to prevent the clay from sticking. Both these materials were stored in open bins adjacent to the moulding benches so that each manipulation of the mould produced a cloud of dust. The patient had been exposed to this dust for 17 years. He suffered from rheumatoid arthritis for 12 years: his father had also been a victim of the disease. The X-ray film of the chest shows the very characteristic appearance of Caplan's syndrome.

5 other cases of pneumoconiosis have been discovered by mass radiography surveys; 2 of them in women. The present case is the first example of Caplan's syndrome reported in this occupation. *Charles L. Sutherland*

Brink, G. C., Grzybowski, S. G. & Lane, G. B. **Silicotuberculosis.** *Canadian Med. Ass. J.* 1960, May 7, v. 82, No. 19, 959–64, 4 figs. [22 refs.]

159 cases of silicosis and silicotuberculosis in ex-gold-miners in Ontario were investigated and treated at the Timmins chest clinic, over a period of 2½ years. Routine sputum examinations revealed 55 positive cases, 21 on smear and 34 on culture. Stress is laid on the unexpected finding that positive results were associated with a radiographic picture of nodulation or nodulation with indefinite conglomeration as frequently as with conglomeration or massive shadowing. Silicotuberculosis is an extremely chronic disease: the occasional single positive sputum culture result, followed by a number of negative

findings may be regarded as one of its features. In all the 7 cases with cavitation, the sputum was repeatedly positive.

The treatment given consisted of isoniazid, PAS and streptomycin administered in 2 drug combinations, largely because of intolerance to PAS. Treatment was continued for 24 months or longer in the 30 cases with repeatedly positive findings. 26 of these showed sputum conversion.

The tuberculin test in 2 doses, was used to decide suitability for treatment.

(1) Those with positive sputum have positive reactions to tuberculin and should have prolonged treatment. They should be treated in sanatorium because they are a danger to others. They will become sputum negative with treatment. Cases with cavitation may not respond and surgical treatment may be employed.

(2) Those with negative sputum but a positive tuberculin reaction should have prolonged preventive antimicrobial treatment unless they give toxic reactions. Sanatorium treatment is not advised for these cases.

(3) Cases with negative sputum and negative tuberculin reaction are considered not to be tuberculous, whatever the clinical and radiographic findings. Antimicrobial treatment should not be given.

Treatment in most cases had no effect on the radiographic appearance, although in 9 cases there was improvement; in 7 of these the sputum was repeatedly positive. Some patients claimed to be improved by treatment: such improvement, however, might be a psychological effect. Vital capacity and one-second vital capacity measurements were taken and were found uninfluenced by treatment. *Charles L. Sutherland*

BRITISH MED. J. 1960, Apr. 30, 1345–51, 12 figs. (7 on 2 pls.) **Complications of Asbestosis demonstrated at the Postgraduate Medical School of London** [HUGH-JONES, P.; HEARD, B. E.]. Discussion 1351–3.

Hugh-Jones described the history and clinical findings and Heard the post-mortem appearances in a case of asbestosis affecting a man aged 50 who had worked with asbestos for 11 years. The asbestosis had caused honeycombing in peripheral parts of the lungs, principally the left where the lower posterior subpleural zone, the diaphragmatic surface, and to a small extent the anterior surface and apex were affected. A columnar-cell carcinoma was present in the posterior segment of the right lower lobe, and there were numerous metastases in the lungs, hilar glands, liver, brain, adrenals and bones. In addition there were present rheumatic heart disease and old rheumatoid arthritis.

The detailed presentation of the case was followed by a full discussion. Hugh-Jones, referring to the radiological appearances, stated that specific changes may be absent in some cases of undoubted asbestosis, and that in such cases pulmonary function tests provided useful diagnostic evidence; it seemed reasonable to deduce the presence of asbestosis where, in addition to a history of exposure to asbestos, the patient was found to have interstitial fibrosis causing alveolar-capillary block, finger clubbing and chest rales, whether or not the X-ra film showed characteristic changes. Heard referred t the interesting problem that, in this and other cases o asbestosis, the distribution of the fibrosis does not alway correspond to the distribution of asbestos. The 12 illu strations include 7 excellently reproduced on a specia plate. *A. T. Doig*

YOSHIKAWA, M. [**Experimental Asbestosis in Guine Pigs and Rats.**] *J. Sci. of Labour.* Tokyo. 1960 Apr., v. 36, No. 4, 182–95, 18 figs. on 4 pls. [1 refs.] [In Japanese.] English summary.

The following is taken from the summary in English The author used guineapigs and rats, and induce asbestosis by the technique of compulsive inhalation o asbestos fibres in saline. There was a high mortalit soon after inhalation, due to asphyxia from obstructio of relatively large bronchi and to atelectasis and pneu monia from obstruction of smaller bronchi.

The essential changes proved to be non-specific alveo litis with giant cells and formation of asbestosis bodies in rats, but not guineapigs, there was no proliferation o collagenous fibres in the fibrous lesions. The finding o asbestosis bodies in rats is regarded as new. It ha formerly been assumed that asbestos fibres less than 5 in length are harmless, but the author's findings sugges that this is not true. *Charles Wilcocks*

D'ANS, A. M. & MÜLLER, H. A. Elektronenoptische Befunde an Staubpartikeln einer Talklunge. [**Elec tronoptical Findings in Dust Particles in a Tal Lung**] *Arch. f. Gewerbepath. u. Gewerbehyg* 1960, v. 18, No. 1, 107–8, 3 figs.

SEN GUPTA, A., FERRIS, B. G., Jr. & RAO, M. N **Oxygen Consumption of Male Indian Jut Workers.** *Arch. Indust. Health.* Chicago. 1959 Aug., v. 20, No. 2, 96–9, 1 fig.

The metabolic cost has been ascertained in 46 worker selected at random from various processes at a jute mil in West Bengal. The Douglas bag and the Haldan method of gas analysis were used. The oxygen consump tion varied from about 1,200 in stockpiling to 200 cc. pe minute in sack-sewing. Correlation between oxygen con sumption and minute volume was high but between oxy gen consumption and pulse rate was low, perhap because of low oxygen consumption in many of thes jobs and varying levels of heat stress at the time o examination. *M. L. Thomson*

BRITISH STEEL CASTINGS RES. ASS. **Data Sheets o Dust Collectors.** 2nd (revised and enlarged edition. pp. vii. + 39, illustrated. 1960, Mar Sheffield 2: East Bank Road. [30s.]

Many different types of dust collectors have bee introduced to the market under various trade names i recent years, and it becomes increasingly difficult fo potential users of such equipment to keep abreast o

developments in this field. This series of data sheets has been compiled to facilitate the selection of the most suitable unit for a particular purpose. It gives details of 32 dust collectors, and as far as possible the collection efficiency, pressure drop, and water usage of each type of collector are clearly indicated. For each appliance a diagram showing the principle of operation is given.

An introductory chapter includes comments on types, selection, location and approximate cost of dust collectors, as well as a series of efficiency curves. In connexion with most of the collectors described examples of installations are mentioned, with information as to the capacity of the collectors in use and the type of dust dealt with.

Although the appliances described are suited primarily for application in steel foundries, this book should be of interest to those concerned with dust problems in other industries. *Thomas Bedford*

FAY, J. W. J. **Experiments with the Hexhlet Dust Sampler in British Coal Mines.** *Ann. Occup. Hyg.* London. 1960, Apr., v. 1, No. 4, 314–19, 1 fig.

Most of the samples of airborne dust taken in connexion with the National Coal Board's Pneumoconiosis Field Research have been collected with the thermal precipitator. Normally the concentrations are calculated in terms of the numbers of particles from 1 to 5μ in size, and a visual estimation is made of the proportion of coal particles to particles of other minerals in that range of size.

It is desired to collect samples yielding sufficient dust of this "respirable" size to allow of systematic compositional analysis, and for this purpose field trials have been carried out with the Hexhlet dust sampler [this *Bulletin,* 1955, v. 30, 520]. This instrument consists of a soxhlet-thimble sampler driven by compressed air and fitted with a horizontal elutriator with a theoretical "cut-off" of 50% at 5μ diameter for particles of unit density. Thus the sample consists of two fractions, the "respirable" dust (essentially below 5μ) in the soxhlet thimble, and the heavier fraction (above 5μ) in the elutriator. The sampling rate is 100 litres per minute.

Four of these instruments have been used in various collieries, and parallel samples have been taken with the long-running thermal precipitator.

The trials were designed (1) to examine the composition of dusts arising from selected operations, and to compare the respirable and elutriated fractions; (2) to investigate the variation in the composition of dust on the coal face with time; (3) to investigate the accuracy of the present routine method of estimating the proportion of non-coal particles by visual discrimination on thermal precipitator slides; and (4) to investigate the relation between the mass concentration of respirable dust and the corresponding particle count in coalface samples.

There were wide variations in the ash and quartz contents of the different samples. In general the ash and quartz contents of the elutriator fractions were higher than those of the corresponding thimble fractions. There was a tendency for the coalface samples of thimble dust collected on coalgetting shifts to have lower ash and quartz contents than those taken on other shifts. On the whole, the ash and quartz contents of samples taken in headings were higher than those found in the samples taken on coalfaces.

In a series of samples taken on the coalface there was little variation in the composition of the dust with time. Such variations in composition found in samples taken in a heading were related to the composition of the rock through which the heading was being driven.

Comparison of the measured ash content of the thimble dust with the estimated proportion of non-coal particles in the corresponding thermal precipitator samples showed that the standard of visual discrimination was reasonably good.

In these experiments a numerical concentration (thermal precipitator) of 1,000 particles (1 to 5μ in size) per cc. of air corresponded with a mass concentration (thimble sample) of 25 mgm. of dust per cu.m. of air.

It is concluded that the standard Hexhlet instrument is suitable for obtaining occasional important samples for research purposes, but is not suitable for routine use in an extensive systematic programme. *Thomas Bedford*

DONATO, R. J. **Discrimination between Rock and Coal Particles in Thermal Precipitator Samples of Respirable Dust.** *Ann. Occup. Hyg.* London. 1960, Apr., v. 1, No. 4, 280–90, 4 figs. on 5 pls. [16 refs.]

In the examination of samples of airborne dust obtained in coal mines with the thermal precipitator it is often desirable to discriminate between rock and coal particles. The author reviews the various possible ways of doing this, and describes two methods in detail. One of these is an incineration method for use with a densitometric evaluation, and the other is a microscopical technique in which modified dark-field illumination is used.

Both these methods were used successfully in discriminating between rock and coal (or between coal and non-coal) particles in thermal precipitator samples prepared in the laboratory. It is concluded that of the two the incineration method with densitometric counting is much the simpler, and lends itself the more readily to routine analysis where estimates of concentration are wanted on a comparatively large scale. The microscopical method would be used only where detailed investigation of individual particles was necessary, *e.g.,* to determine whether a given particle was a mixture of rock and coal, and, if so, how much of its surface was rock. Particles smaller than 1μ can be assessed with considerable confidence, and the lower limit of size is probably about 0·5μ.

Thomas Bedford

WINKEL, A. Über die Staubmessung am Arbeitsplatz und ihre gewerbehygienische Beurteilung. **[Measurement of Airborne Dust and the Judgment of its Significance in Industrial Hygiene]** *Staub.* Düsseldorf. 1960, May 1, v. 20, No. 5, 156–60, 1 fig. [13 refs.]

Owing to continual fluctuations of concentration, particle size and chemical or mineralogical constitution it is

difficult to measure accurately the airborne dust in industrial premises. In this paper 3 methods are described in detail and compared with regard to their relative advantages and failings.

The latest German Konimeter HS, manufactured by Sartorius-Werke, is giving satisfaction and it is evident that many of the deficiencies of earlier konimeters have been eradicated. Samples are deposited in a fraction of a second so that many can be taken and a table is given which shows the number of samples, spaced at equal time intervals, which is necessary if a reliable idea is to be obtained of the average concentration in a cloud of dust which lasts for any time between 3 and 240 minutes; this is based upon the experiments of HASENCLEVER who was responsible for the development of the Konimeter HS [this *Bulletin*, 1957, v. 32, 775].

It is claimed that the shape of the jet of the instrument is such that few particles exceeding 5μ can pass through and that there is no break-up of aggregates in transit. [The means by which this size-selecting property is achieved is not explained but if it is because the larger particles strike the sides of the jet on entering one would expect that trouble with fragments and blow-off might well occur with some dusts.] The impaction efficiency is stated to be nearly 100% down to 0·5μ but no experiments are quoted which prove this figure to be genuine for the smallest sizes and not due to the break-up of larger particles.

Coating the konimeter slides with white vaseline has to be carried out carefully if accurate dust counts are to be obtained. The microscope incorporated with the instrument is only intended for a rough evaluation of dust concentration; examination of the plates in a projection microscope permits the counting of particles down to 0·7μ and resolution is improved by washing away the vaseline film. Quartz plates are available for use when the sample has to be ashed for mineralogical tests. Samples of either 2·5 or 5 cc. can be aspirated; the larger volume always gives dust concentrations a few per cent. lower than the smaller.

The thermal precipitator, in contrast to the Konimeter HS, takes a sample of long duration from 15 minutes to one hour. The velocity of the air flow into the orifice is only about 5 cm./minute and it is stated that this has an unfavourable effect upon the accuracy of sampling from moving air, causing a deficiency when the ambient air speed exceeds 0·25 m./second. [The grounds for this assertion, which cannot be accepted, are not mentioned. It has been shown recently that thermal precipitator samples are independent of wind speed over a range from 40 to 1200 ft. per minute (HODKINSON *et al., J. Sci. Instr.*, 1960, v. 37, 182). It is suggested that particles are swept past the orifice by virtue of their inertia at high wind speeds but since the stop-distance of a 5μ sphere of quartz at 0·25 m. per second is only about 1/200 cm. the effect is negligible.]

Comparisons of the Konimeter HS and the thermal precipitator, for quartz dust, have been made by HASENCLEVER [this *Bulletin*, 1957, v. 32, 775] with satisfactory results.

An account follows of gravimetric dust sampling by means of filters. Concentrations of dust in industry are often small so that long exposures are necessary for membrane or electrofilters; the former suffer from hig resistance and the latter are liable to penetratio Fibrous filters have many advantages and the solub Mikrosorban type is commended; the dust is extracte by centrifuging the solution of the filter. The lon sampling time which is usual with filters is an advanta for determining average dust concentrations. Filters a particularly suitable for sampling toxic dusts since th effects on man are not confined to those produced b particles in the respirable size range. Sedimentatio analysis can be employed to separate the particles belo 5μ for work on silicosis but this considerable compl cation of the analysis is avoided if a selective samplin device is used, preceding the filter, such as a cyclone horizontal elutriator.

In assessing danger to health relative to dust concen tration the first guide is the 1958 list of MAK value published by the BUNDESMINISTERIUM FÜR ARBEIT UN SOZIALORDNUNG, which includes toxic dusts but not thos causing silicosis and asbestosis.

For silicosis it is best to deal with number concentra tion, rather than weight, including only particles smalle than 5μ diameter (3μ is used in France). Derived fro American figures the following formula relates the max mum permissible number concentration of particles t the quartz content of the dust:

$$\log 10\ T + 0{\cdot}015\ A = K,$$

where T is the number of particles per cc. in the rang 0·7–5μ diameter, A is the percentage of free silica an K is a constant, about 3·3.

The mean particle size in quartz dust fractions belo 5μ has been found to lie between 1·5 and 2μ. By usin the lower figure in the equation, mass concentration i particles under 5μ is related to quartz content as follows

Dust concentration	*Permissible content of free silic in the fraction* 0–5μ
<1·5 mgm./m³.	0·75 mgm./m³.
1·5–2·5	0·5
>2·5	0·25

C. N. Davies

BINEK, B. Szintillationsspektralanalysator für Aerosol teilchen. [**A Scintillation Spectrometer Apparatu for Aerosol Particles**] *Staub.* Düsseldorf. 196 June 1, v. 20, No. 6, 184–5, 7 figs.

The English summary appended to the paper is a follows:—

"An apparatus operating on the spectrometric prin ciple is described with which aerosol particles of suitabl chemical composition can be counted and measured wit recording of size. Its range of application covers bas cally fundamental questions in aerosol research. (Coagu lation, sedimentation efficiency of filters, etc.). Finall an attempt is to be made to employ the apparatus fo rapid chemical analysis of aerosol particles."

MEIKLEJOHN, A. **The Origin of the Term "Pneu monokoniosis".** *Brit. J. Indust. Med.* 1960, Apr v. 17, No. 2, 155–60.

The author has translated the relevant passages of paper in German on Diseases of the Lungs due to th

Inhalation of Dust, by Friedrich Albert von Zenker, published in 1867 (not 1866 as usually stated). In this Zenker coined the word pneumonoconiosis after describing a woman patient with siderosis. *Charles Wilcocks*

PERNIS, B. & MAGISTRETTI, M. **A Study of the Mechanism of Acute Hemolytic Anemia from Arsine.** *Med. d. Lavoro.* 1960, Jan., v. 51, No. 1, 37–41, 4 figs.

The object of the experiments, which are indicated briefly, was to see whether the haemolytic action of arsine is the result of its causing reduced glutathione to disappear from erythrocytes. It is known that sulphydryl groups of glutathione (GSH) are essential for the maintenance of intact erythrocyte structure, that decrease of erythrocyte glutathione increases the rate of haemolysis in shed cells and that some inhibitors of GSH are haemolytic.

Washed human erythrocytes were incubated with solutions of AsH_3 ranging from 5×10^{-4}M to 1×10^{-4}M. The rate and degree of haemolysis, plotted at intervals for 4 hours as the percentage of haemolysis, were directly proportional to arsine concentrations. Haemolysis began, after inversely proportional latent periods of 20 to 40 minutes, when the GSH dropped to 40% of its initial value. When reduced glutathione was added in excess of the amount required for binding GSH to arsenic, haemolysis did not take place, the curve being similar to that produced by adding 0·9% NaCl to erythrocytes.

With the weaker arsine solutions, haemolysis was not complete. Theoretically those erythrocytes which contained most reduced glutathione should be the more resistant to arsine. Young erythrocytes have a higher content than old cells. Haemolysis curves of whole blood erythrocytes and of younger and of older cells, which were separated by sedimentation in plastic tubes, show the younger erythrocytes to be the most resistant and the older cells the least.

When a solution of GSH was incubated with AsH_3 in the presence of 0_2, there was progressive disappearance of GSH which suggested a catalytic action by the arsenic, transforming the GSH to oxidized glutathione, rather than the formation of a complex between the 2 compounds.

The correlation between the fall of GSH and haemolysis indicates that the haemolytic activity of AsH_3 is due to its ability to decrease erythrocyte GSH.

M. Patricia Fitzsimons

VANCE, G. H. **Cadmium Exposures in Silver Soldering Operations.** *Amer. Indust. Hyg. Ass. J.* 1960, Apr., v. 21, No. 2, 107–9, 2 figs.

In various plants throughout Connecticut, silver soldering was shown to be a source of cadmium or cadmium oxide fume—in excess of the Threshold Limit Value (TLV) of 0·1 mgm. cadmium per m³, particularly where the heat source was an oxyacetylene torch, with its high temperature, 6000°F., and excess 0_2 in the flame, and also where small pieces were soldered. In large pieces, heat conduction controls temperatures. Silver soldering is essentially a low temperature brazing process for bonding silver, copper, brass, bronze or stainless steel. The solders may be composed of alloys of silver, copper, zinc and cadmium. Other heat sources were an induction heat unit or oven, where the amperage is adjusted to provide the solder flow point, 1175° to 1295°F., and a gas-air torch, 3500°F.

Air samples were collected at 1 cu. ft. per minute and analysed by the polarographic method. A table gives breathing zone and atmospheric concentrations of cadmium, percentage of cadmium in each solder and type of heat source and work. No correlation was found between atmospheric concentration and cadmium solder content, 14–25%. Breathing zone concentrations where oxyacetylene torches were used were all above the TLV except in brass tube assembly; in sunglass assembly they reached 0·38 mgm. per m³, and with plumbing goods 1·3, but were reduced subsequently by shielding. Where the other heat sources were used, these concentrations were below the TLV, except with a triple burner gas-air torch in oil burner manufacture and with a resistance unit, before installation of glass shields, in sunglass frame work.

Mechanical exhaust ventilation is recommended for oxyacetylene torch silver soldering and it may be advisable with the other heat sources.

M. Patricia Fitzsimons

UNITED KINGDOM ATOMIC ENERGY AUTHORITY. **Industrial Group. Information Bibliography: Beryllium Health Hazards and Protection** [CHADWICK, U. R. M.]. 29 pp. 1959. I.G. Information Series 37 (RD/R). H.M. Stationery Office. [3s.]

"This is a comprehensive selection of some 222 references to classified and unclassified literature on the subject and includes a selection of general references on the properties, uses and fabrication of the metal. The references were obtained from the U.K.A.E.A. abstracts index to classified British, Canadian, and American reports, and Nuclear Science Abstracts (to June, 1958)."

DOMNITZ, J. **Thallium Poisoning. A Report of Six Cases.** *Southern Med. J.* 1960, May, v. 53, No. 5, 590–93. [15 refs.]

Thallium compounds nowadays employed as pesticides have caused many accidental poisonings and have been used with suicidal and homicidal intent.

A report is given here of 6 cases of thallium poisoning, proved by toxicological investigation, in which the source of the poison was known in 4 instances but unknown in 2. The thallium was ingested as "roach" poison in tablet or liquid form or rat poison fluid. The liquids had been taken accidentally or with suicidal intent. The symptoms were gastrointestinal, either mild or severe, in 2 patients. Initial symptoms indicative of encephalopathy and peripheral neuropathy existed in 3 patients. Alopecia or easy epilation occurred in 5. In all instances

the diagnosis was confirmed by chemical analysis of urine, or also of blood and faeces. There were 2 deaths and in these thallium was found in many of the body tissues. In a man of 49 years who had swallowed rat poison the highest levels of thallium found were in the blood (17 mgm. per 100 cc.) and in bone (16·14 mgm. per 100 gm.).

There is a review of the "pertinent literature on thallotoxicosis" and some account of the chemical and physical properties of thallium and its salts.

Methods of therapy are considered also with mention of the use of BAL and CaEDTA in the treatment of thallium poisoning, which have yielded "encouraging but inconclusive" results. *M. E. Delafield*

VIGNOLI, L., CRISTAU, B., DEFRETIN, J. P. & VIGNOLI, R. Observations au sujet de l'emploi de tubes réactifs types Draeger pour le dépistage de l'oxyde de carbone sanguin. [**Use of Draeger-Type Tubes for the Detection of Carbon Monoxide in the Blood**] *Arch. Malad. Professionnelles.* Paris. 1960, Apr.–May, v. 21, Nos. 4/5, 201–4.

HENSCHLER, D., STIER, A., BECK, H. & NEUMANN, W. Geruchsschwellen einiger wichtiger Reizgase (Schwefeldioxyd, Ozon, Stickstoffdioxyd) und Erscheinungen bei der Einwirkung geringer Konzentrationen auf den Menschen. [**Olfactory Thresholds of some important irritant Gases (Sulphur dioxide, Oxone and Nitrous oxide) and Symptomatic Effects of Low Concentrations in Man**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 17, No. 6, 547–70, 5 figs. [Numerous refs.]

The sense of smell can serve as the first intimation of concentrations of gases which, in workplaces, may cause discomfort and irritation without injury to health, and complaints of odour in dwelling places. A review of the literature on the effects of low concentrations of SO_2, ozone and "nitrous gases" includes a comparison with the Maximum Allowable Concentrations of these substances at present recognised in U.S.A. and Germany. The MAC is given as 5 p.p.m. for SO_2, 0·1 p.p.m. for ozone, and 25 p.p.m. for nitrous gases, while the olfactory thresholds range from 0·3 p.p.m. to 30–37 p.p.m. (catarrh and cough) for SO_2, 0·1 (perceptible by smell) to 9·2 p.p.m. (headache, drowsiness and lung oedema) for ozone, and from 2·5 ("visible signs of chronic poisoning") to 62 p.p.m. (laryngeal irritation and thirst) for NO_2.

The authors studied the response of persons inhaling for half an hour without masks or tubes, in a closed room, air containing increasing concentrations of the 3 gases, with conditions of varying relative humidity.

With SO_2 at 1·1 p.p.m., both smell and taste were noticed by 7 out of 12 persons; only 4 were able to recognize the gas; the taste was described as "metallic", and increased with increasing concentrations. 2·6 p.p.m. became unpleasant at the end of half an hour; 5 p.p.m. caused coughing.

For ozone the olfactory threshold, described as "electric" smell, was less than the lowest concentrati used (0·02 p.p.m.); at 0·28 p.p.m. there was slight irritati and dryness of the nose and throat; at 0·58 p.p.m. cou at 0·9 p.p.m. sneezing and tightness of the skin of face, and at 1·2 p.p.m. marked increase of all sympto

NO_2 was perceptible by odour at 0·1 p.p.m. but w increasing concentrations up to 20 p.p.m. tolerance v established so that neither odour nor irritation was not This rapidly acquired tolerance to relatively high conc trations of NO_2 emphasizes the adequate warni property of nitrous gases.

Increasing the relative humidity from 60–80% increas the irritative symptoms of NO_2 but had no definite eff on the other two gases.

It is concluded that the maximum concentrations wh can be tolerated without discomfort for long periods a for SO_2, below 0·5 p.p.m., for ozone, below 0·05 p.p. and for NO_2 below 1 p.p.m.—about one-tenth of recognized maximum allowable concentrations.

Ethel Browning

GOLDSTEIN, I. & POPOVICI, Carmen. Modifications la catalase et de la péroxidase dans l'intoxicati experimentale au nitrobenzène. [**Catalase a Peroxidase Alteration in Experimental Nitr benzene Poisoning**] *Med. d. Lavoro.* 1960, Ja v. 51, No. 1, 42–8. [21 refs.]

Enzyme activity was measured to investigate t mechanism of nitrobenzene poisoning, not explained methaemoglobinaemia because reduction of this in earl experiments did not reduce mortality rates [this *Bullet* 1960, v. 35, 439]. 635 serial determinations were ma of blood catalase activity in 124 rats, at first for 1 d and then for 4, and 251 of erythrocyte peroxidase activ in 63 rats. Poisoned rats were injected subcutaneou with a single LD50 dose of nitrobenzene, 0·64 gm. p kgm. of body weight. In each animal, at intervals, en matic activity was calculated as a percentage of its init activity. Results in poisoned and control animals a presented in tables as serial mean percentages, and t number in each group, standard deviations, mean erro and tests of significance are included.

Catalase activity decreased continuously to 76% in day and to 67·1% in 4, in the poisoned animals. T controls' activity fell slightly, but in the 4 days' expe ments the differences were significant. To investig whether these results were due to catalase inhibition haemolytic anaemia or both, the catalase index was es mated in a 1% solution of washed erythrocytes 96 ho after poisoning. In controls it remained almost consta in the poisoned animals it fell to 86·6%, a significa decrease. [Figures in the table appear to be transpose The decrease of blood catalase activity in nitrobenze poisoning is due, in part at least, to enzyme inhibiti The continuous fall suggests persistence of toxic eff and it is possible that this test could be useful wh methaemoglobinaemia is slight or absent.

There was some decrease in peroxidase activity, t significance of which is discussed and is being inves gated further. *M. Patricia Fitzsimons*

ROUBAL, J. & KRIVUCOVÁ, M. Hygienische Probleme bei Verwendung von tertiärem Butylchromat als Passivierungsinhibitor der Metallkorrosion. [**Hygienic Problems in the Use of Tertiary Butyl Chromate as an Inhibitor of Metal Corrosion**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 17, No. 6, 589–96, 2 figs.

The protective action of certain oils and vaseline in metal production is increased by the addition of soluble chromic acid derivatives, which inhibit metal corrosion.

As a result of complaints of giddiness and gastric discomfort from a laboratory assistant engaged in packing metal articles in paraffin-impregnated paper containing 5% of tertiary butyl chromate, animal experiments were carried out in conditions intended to reproduce as far as possible those of the laboratory. The air over the apparatus was found to contain 2·4 μgm. of Cr^{VI} per litre, but the surrounding air only traces.

White rats were exposed to inhalation of air in a vessel into which a filter paper impregnated with butyl chromate and butyl alcohol was placed. The exposure, for 30–60 minutes, was repeated, usually every day.

Necrosis of the skin and subcutaneous tissues developed within 12 hours. The lethal dose was 3 ml. of the mixed fluid for a 60-minute exposure. Symptoms included drowsiness, "on side" prostration, muscular weakness and twitchings, ataxia, loss of weight, and rapid superficial respiration; these sometimes disappeared 1 hour after cessation of exposure but death took place 4 days later. With a dose of 2 ml. for 60 minutes the symptoms were milder—signs of irritation, lachrymation, rapid respiration and ataxia. Histological examination showed extensive epithelial exudation in the lung alveoli, haemorrhage and fat deposition in the liver and, in the less severely affected animals, hyperaemia and vacuolation of the liver cells.

A comparison of the toxic effects of butyl alcohol and butyl chromate was made by separate inhalation experiments. The animals in the butyl alcohol group showed slow respiration, rapid narcosis, and no lachrymation, while the butyl chromate group showed slow but not total narcosis and rapid difficult respiration. The lungs of the butyl alcohol animals also differed in showing no oedema, cellular exudation or bronchial inflammation.

It is concluded that butyl chromate in certain industrial conditions can cause pneumonic changes, narcosis and necrotic lesions of the skin. Atmospheric concentrations should never be greater than 0·1 μgm. per litre CrO_3; contamination of the skin should be avoided; closed apparatus for mixing with paraffin and with automatic filling should be used, and special care taken with the finished product; when paper impregnation is carried out in a paper calendar machine at temperatures of 50° to 70°C. those parts of the machine where the temperature is higher than 20°C. should be enclosed and provided with exhaust ventilation. *Ethel Browning*

HENSCHLER, D. Neuere Untersuchungen zur Toxizität von Triarylphosphaten. [**Observations on the Toxicity of Triarylphosphates**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1960, Apr., v. 10, No. 4, 86–8.

Triarylphosphates are essential for many technical purposes. The most frequently used type of preparation was at one time tricresylphosphate containing about 30% of o-cresol which in Germany caused many cases of irreversible paralyses particularly in the war and post-war periods. Much less toxic preparations of lower o-cresol content have now been introduced. For many purposes triarylphosphates in which cresol is more or less replaced by a homologous group can be used. The author, who has published observations on the toxicity of these preparations [this *Bulletin*, 1959, v. 34, 352], discusses the relation between chemical configuration and toxicity and reports the results of some experiments on hens with a number of different arylphosphates to determine the single dose which would induce signs of paralysis. The preparations tested were 2 tricresylphosphates (1 containing 26·7% and the other 3·3% of o-cresol), 2 diphenylmonocresylphosphates, a diphenylmonoxylenylphosphate and a product called a technical xylenol mixture. The last of these which contains 21·8% of 3, 4-xylenol, 32·8% of 3,5-xylenol, and small amounts of o-cresol (1·6%) and phenol (0·7%) was found to have a very low toxicity as compared with that of the other tested preparations. It is considered that there is practically no danger of poisoning in using this material. *M. E. Delafield*

LOB, M. Intoxication mixte par insecticides (organomercuriels et dinitro-ortho-crésol). Essai de traitement par le versénate de calcium. [**Mixed Insecticidal Poisoning (Organic Mercurials and Dinitro-ortho-cresol). A Trial of Calcium Versenate Treatment**] *Ztschr. f. Unfallmed. u. Berufskrankh.* 1960, Mar. 15, v. 53, No. 1, 53–7, 1 fig.

The toxic substances used daily by nurserymen make it likely that numerous cases of poisoning occur which escape legislation. The example quoted shows that it is necessary to warn people who use insecticides and weedkillers of the dangers, to continue the struggle against negligence and to inform those in charge of protective measures. The patient, aged 58 in 1959, had been employed since 1943—treating potatoes and spraying orchards and crops in spring and summer with Dinitro-ortho-cresol mixtures, and handling seeds, treated with mercurials, in autumn. Generally he wore no mask or gloves. When using DNOC he had had attacks of nausea and abdominal cramp.

In summer 1957 he became ill with classical symptoms of DNOC poisoning and abdominal symptoms which disappeared on stopping work. In November, after seed work, his symptoms recurred and he also had the nervousness, irritability and hand tremor of mercury poisoning, and later loss of the power of concentration. By June there was scarcely any improvement though the previously raised basal metabolic rate had become normal. There was now polyuria with albuminuria and the urinary Hg had risen from 51 to 72 μgm. per litre. Later, courses of EDTA had no effect on Hg excretion which continued to decrease steadily to a normal level. In May 1959 the patient was well.

July spraying with DNOC brought about a sudden, more severe illness, with nausea, palpitations, anorexia,

sweating, general malaise, insomnia and the metabolic rate +38%. The intense yellow staining of hair, skin and nails showed a complete lack still of elementary precautions. There is mentioned the possibility that the Hg had sensitized the patient to DNOC or that it had affected excretion. *M. Patricia Fitzsimons*

J. Amer. Med. Ass. 1960, Apr. 30, v. 172, No. 18, 2077–80, 2 figs. [10 refs.] **Occupational Dieldrin Poisoning.** [Report of the Committee on Toxicology (Conley, B. E., Secretary).]

Dieldrin is used for controlling insect pests of crops and forests and in some countries, but not approved in the U.S.A., as a residual spray in dwellings in the control of vector-borne diseases [this *Bulletin*, 1959, v. 34, 1209, 1270]. The dilute formulations accepted by the U.S. Department of Agriculture for indoor use are dieldrin oil solution, 0·5%; dust 1%; and emulsifiable concentrates to be diluted before use. Spray formulations, 0·5%, are marketed.

Dieldrin acts centrally as a stimulant to the central nervous system. It is absorbed especially through the skin, as powder or liquid, and through the respiratory and alimentary tracts. It is stored in fat, the only tissue in which it can be measured at present. Though detoxification and excretion mechanisms have not yet been determined, it is known that it is dissipated from tissues after exposure ceases. However, recurrence of symptoms suggests that dieldrin produces morphological or biochemical lesions.

Oral toxicity is 3–5 times greater than that of DDT and the acute dermal toxicity in xylene is 40 times greater. The acute oral toxicity in rats ranges from 37 to 87 mgm. per kgm. Large amounts in animals cause food refusal, rapid loss of weight and convulsions, always fatal unless treated [*ibid.*, 1958, v. 33, 488]. In man symptoms have followed oral doses of 10 mgm. per kgm.

Clinical experience in other countries is described [this *Bulletin*, 1958, v. 33, 597, 859] and poisoning in a baby of 9 months in Israel, found near insecticide powder containing 4% dieldrin, left over after treating watermelons. Face and mouth were washed. 6 hours later sudden unconsciousness, dyspnoea and cyanosis preceded clonic convulsions of limbs and facial muscles. Even with sedation in hospital they lasted for 14 hours. Horizontal nystagmus was the only other sign. Pyrexia and tachycardia developed before death which occurred 20 hours after poisoning. Plates illustrate central lobular necrosis of the liver and degeneration of kidney tubules —the non-specific changes found in experimental dieldrin poisoning with the pulmonary oedema which follows convulsions. *M. Patricia Fitzsimons*

Aron, E., Neel, J. L. & Groussin, P. Aplasie médullaire avec pancytopénie mortelle par intoxication au thiophosphate de diéthyle et paranitrophényle (Parathion)? **[Medullary Aplasia with Fatal Pancytopenia in Parathion Poisoning]** *Arch. Malad. Professionnelles.* Paris. 1960, Apr.–May, v. 21, Nos. 4/5, 215–18.

Erdmann, W. D. Klinische Erfahrungen mit de Antidot Pyridin-2-aldoxim-methojodid (PAM) b E 605-Vergiftungen. Ausgewählte Kasuistik. **[Th Use of PAM in Cases of E 605 (Parathion Poisoning]** *Deut. med. Woch.* 1960, June 3, v. 8 No. 23, 1014–16, 1032.

The English summary appended to the paper is follows:—

"Selected case reports are presented to delineate th use of pyridine-2-aldoxime methiodide (PAM) as an ant dote against parathione (E 605) poisoning. It is stresse that the use of the antidote PAM does not obviate oth measures, such as high doses of atropine, gastric lavag administration of charcoal, and routine supportive trea ment. Intubation and artificial ventilation may be ind cated. PAM should be administered as early as possib at least 0·5 g. intravenously. This dose may be repeate once after a few hours and, in severe poisoning, yet agai after 24 hours. A knowledge of serum esterase activi (using a rapid test with 'Acholest' paper) is useful i deciding on PAM dosage."

United Kingdom Atomic Energy Authority. **Repor of the Committee on Training in Health an Safety** [Veale, D., Chairman] **to the Authorit Committee on Health and Safety** [Makins, R Chairman], U.K. Atomic Energy Authority, Febru ary 1960. pp. vi + 95. 1960. London: H.M. Sta tionery Office. [5s. 6d.]

After the Windscale accident an independent Authorit was initiated by the Atomic Energy Authority; this wa Sir Alexander Fleck's Committee on the Organizatio for Control of Health and Safety in the U.K. Atom Energy Authority. One of the recommendations of th Fleck Committee was that the Authority, as th vanguard of the nation's effort, should assume respons bility for building up the national supply of healt and safety specialists and establish a national trainin centre for health physics and nuclear safety staff.

The Authority in their turn arranged for the forma tion of another independent Committee to advise abou these new responsibilities and Sir Douglas Veale ha acted as Chairman of a Committee which has sat for 2 months. As stated in the foreword, "The Committee study of these problems on a national scale led them t consider matters outside the Authority's competence" those not within it "are now referred to the appropria Government departments." The Committee has alread made two interim reports on postgraduate training an background training included in the present issue, an in addition has made recommendations (Chapter IV pp. 29–32) as to the means whereby the services of high trained specialists may most effectively be provided.

The report contains 10 chapters and appendices A– which cover practically every field calling for expe attention in matters relating to the public safety again all that is understood in the use of the term when applie to atomic radiation. It is impossible to summarize brief a report of this magnitude, each must dip into it for h own purpose. Of chief medical importance, apart fro day-to-day application of recommendations, is the sectio

devoted to *Training Courses for administrators, managers, medical officers of health and other professional workers* (pp. 43–44). Administrative issues may often be more perplexing than the technical issues—hence the importance of adequate background training for those who have to be able to take related policy and managerial decisions. A pilot course for administrative and managerial staff was arranged at Oxford in 1959 lasting a fortnight. This was attended by senior civil servants, medical officers of health, officers of the three services, managerial and executive staff from industry (nationalized and private) water engineers, river board authorities and a trade union official. The list is given here to indicate the wide reach of the efforts for safety.

The whole report is a most valuable one.

S. Russ

POST OFFICE. **Safety Precautions relating to Intense Radio-Frequency Radiation.** 8 pp. 1960. London: H.M. Stationery Office. [9d.]

The safety precautions described comprise a set of recommendations designed by their observance to prevent harm to the body from radio-frequency apparatus giving radiation in the range of 30–30,000 Mc/s. The recommendations apply to all classes of fixed and mobile radio transmitting stations (broadcasting, radio navigation and radar) and to radio equipment used for scientific and industrial purposes.

The quantitative basis of the recommendations derives from *Recommendations of the Medical Research Council* and briefly is as follows:—

For the range already stated the upper permissible limit for continuous daily exposure is 0·01W/sq. cm., and in the case of pulse modulation systems the radiation should be averaged over complete trains of pulses including any intervals between pulse trains. There are a number of recommendations designed to protect the public from venturing too near to operating machines.

The basic characteristics of measuring equipment for detecting this radiation are given in Appendix I without any specified set-up (pp. 7–8).

The Report should be in the hands of all those responsible for employing radiation apparatus of this kind; the recommendations are singularly devoid of difficulty in putting into practice. *S. Russ*

BELL, A. **Radiation and the New South Wales Department of Public Health.** *Med. J. Australia.* 1960, Apr. 9, v. 1, No. 15, 568–72. [10 refs.]

The New South Wales Radioactive Substances Act, which incidentally binds the Crown, was assented to in March 1957. Under this Act a Radiological Advisory Council was set up whose main initial function was to produce regulations. Present legislation requires users of either radioisotopes or certain X-ray machines to be licensed; they are reviewed yearly.

The importation of radioisotopes into Australia is restricted under the Customs (Prohibited Imports) Regulations. Approval to import is given only after the Commonwealth X-ray and Radium Laboratory is convinced that the isotope will be used safely and usefully. The imports are considerable; for the period July 1, 1957 to July 30, 1958, 656 shipments were made totalling about 159,000 mcs. The greatest users were the industrialists with medical and scientific bodies using very much less.

The permissible doses of ionizing radiation listed in Table III are doses which in the light of present knowledge, are not expected to cause appreciable bodily injury to a person at any time during his lifetime.

This review of the present situation in the State of New South Wales is a comprehensive one, every feature of countering the hazards of ionizing radiation being dealt with. This should make it a valuable reference as an example of the present-day attitude taken by one of the chief States in Australia. *S. Russ*

HOOPER, F. M. **Radiation Hazards in X-Ray Diagnosis.** *Med. J. Australia.* 1960, Apr. 9, v. 1, No. 15, 572–6. [18 refs.]

The author states at the outset "This paper will discuss injuries which are caused or thought to be caused by small doses of X-rays. In particular . . . genetic hazards and the production of malignant disease."

Given the undisputed fact that X-rays can produce mutations, and further the fact that most mutations are harmful, a good start can be made in any campaign which would raise public alarm against the use of X-rays. There have been several occasions of this sort and the author has done a service by drawing attention to the doses of X-rays received, for instance, by the gonads for a number of common representative radiological exposures. The doses are insignificant except those in and close to the female pelvis and those in the male pubic region.

He quotes a number of authors who reviewed the literature recording several thousand pregnancies following radiotherapy to the ovaries with doses of 50 to many hundreds of gamma. In this series the number of congenital abnormalities and miscarriages was no larger than could reasonably be expected in a comparable normal population. Over-estimating the risk of radiological examinations will lead to denying a patient a valuable procedure. The production of malignant disease by X-rays has resulted in the loss of life among radiological pioneers, but the author is concerned with present-day possibilities of malignant disease following up on X-ray diagnostic procedures. He is inclined to credit the claim that radiological examination of a pregnant woman may lead to malignancy in the offspring, particularly leukaemia.

The author then proceeds to give some excellent hints about safety methods in X-ray diagnosis and takes a very hopeful view of the situation provided one does take proper precautions.

His final words on the subject may be a useful corrective to exaggerated statements over essential X-ray dangers. He writes "The greatest real hazards in X-ray diagnosis are, and always have been, incomplete examinations and inaccurate diagnoses. These are the hazards that rightly claim most of our attention." *S. Russ*

LENGER, V. J. & KUDRNA, J. **The Influence of a Change in Production Technology on the Incidence of Radiation Hazards.** *Ann. Occup. Hyg.* London. 1960, Apr., v. 1, No. 4, 291–8, 6 figs.

This paper, originating from the Institute of Industrial Hygiene and Occupational Diseases in Prague, is important in two main respects. It draws attention to the importance of morale in radioactive work-places and describes the general design and function of instruments used by the visiting physicist in detecting and measuring unwanted radiation. The authors make a very important point when they say that there is a diminished morale when the work in hand is not a central point of interest in the establishment and represents only one subordinate link in a chain of complicated processes. This psychological outlook is rather common even with the supervisors.

The reference in the present instance is to the methods of safety existing among those working with radioluminous substances. Until quite recently the active agent used has been radium but there is now added ^{90}Sr in order to increase the luminosity of the article. This is probably a greater hazard if taken into the body than is radium. It has been shown over and over again that the manipulation of luminous compound has to be watched with the most minute care if the hazards to health are to be countered. One case of radiodermatitis on the back of the fingers of the right hand of a woman applying this paint is reported and the carrying of detectable radioactivity to a worker's home is good evidence for the tightening up of the regulations. The article is illustrated by diagrams and photographs of the detecting instruments. *S. Russ*

BLACK, R. H. **Protecting and Cleaning Hands contaminated by Synthetic Fallout under Field Conditions.** *Amer. Indust. Hyg. Ass. J.* 1960, Apr., v. 21, No. 2, 162–8, 4 figs. [10 refs.]

Radioactive contamination of the skin following a nuclear weapon detonation may pose a difficult health problem for though it is easy with a good scrub of soap and water to get a lot of it off the body, it is the fraction left behind that has to be dealt with.

The paper is the result of a field study simulating the conditions of nuclear weapon detonation. The material used was Lanthanum-140 which was mixed with the soil. A selected operating personnel was given the experimental protection of a barrier cream before entering the contaminated area. Anyone returning from this area with over 500 counts (Geiger Muller) per minute on his hands was directed to the hand cleaning centre. Here a considerable number of cleansing agents were employed to de-contaminate.

The most generally successful was EDTA. It was found that the waterless hand cleaner showed the same effectiveness as soap and water.

This was an exhaustive series of tests, well documented, but no one method has been found which does away with the need for a final check after washing to see whether permissible levels have been exceeded. *S. Russ*

V. PREYSS, J. A. Zur Beurteilung des Bäckerekze **[Contribution to the Evaluation of the So-Cal Baker's Eczema]** *Berufsdermatosen.* Aulendo 1960, Apr., v. 8, No. 2, 68–72.

In this short paper there is an account of the le prohibitions in Germany in regard to additives in flo There is a list of the chemical substances used bleachers and improvers of flour which have to be c sidered in relation to baker's eczema. Of these s stances persulphates are the chief allergens although cent observations suggest that benzoyl peroxide is also importance in this respect.

Since April 1, 1957 when additives to flour such as p sulphate were prohibited in the German Federal Repub the incidence of the so-called baker's eczema has di nished greatly. This is of much importance from viewpoint of occupational skin diseases entitling to co pensation.

In an experience of 70 cases of baker's eczema seen the period 1954–59, it was found by skin testing, t allergy to persulphate was very frequent but that af 1956 no patient though sensitive to persulphate suffer from eczema.

There is a discussion of the importance of this dimi tion in baker's eczema in relation to the nature of oc pation and to compensation. *M. E. Delafield*

BEHRBOHM, P. & BRANDT, B. Allergisches Konta tekzem durch technische und gereinigte Hexachlo cyclo-hexanpräparate bei der Anwendung im Pfla zenschutz und in der Schädlingsbekämpfung. **[A lergic Eczema by Contact with Technical a Purified Benzene Hexachloride Preparatio employed in Plant Protection and Pest Contr** *Berufsdermatosen.* Aulendorf. 1960, Apr., v. No. 2, 95–101, 1 fig.

This is a report on 2 cases of occupational conta eczema in men 1 of whom was employed to apply du and sprays to plants and fields for their protection agai disease and the other to destroy insects and rodents houses and gardens. The history of these 2 men, t nature of their work in the past and the large variety different chemical products with which they had co in contact are described. There are 2 tables which gi the results of skin tests in these men with a large numb of different substances or preparations.

Both men had at some time worked with preparatio containing benzene hexachloride (BHC). The chemic composition of these preparations is described. There a considerable discussion and the main conclusion is th the alpha, beta, gamma and delta isomers of BHC are n sensitizing and that allergic reactions which occur wi some preparations are due to impurities [this *Bulleti* 1960, v. 35, 235]. Skin reactions did not occur with t chemically pure isomers. For some years the farmi industry have employed only high quality BHC whi consists of 99·0% of the gamma-isomer and contains sensitizing impurities. *M. E. Delafield*

GROSDANOV, A. Behandlung allergischer Berufskrankheiten mit Wismut. **[Treatment of Allergic Occupational Diseases with Bismuth]** *Berufsdermatosen.* Aulendorf. 1960, Apr., v. 8, No. 2, 72–80.

In this paper the introduction gives a list of the considerable number of medicaments which are used in the treatment of allergic diseases. There follows a report on the author's experience of the results of treatment of occupational allergies by bismuth carbonate. This substance is administered intramuscularly as a 10% emulsion in oil of which 1·0 ml. is given twice a week for 6–7 weeks. If considered necessary a second course of this treatment is given after a month's rest.

The number of patients so treated was 93 (17 men and 76 women) of whom 60 had occupational eczema, 25 had a professional dermatitis and 8 an occupational asthma. There is a statement of the occupations of these patients and a list of the substances to which skin tests had shown them to be sensitive.

The effect of bismuth treatment is slow and gradual. In most cases improvement is first manifest after 3 or 4 weeks. In most of the patients whose condition is only improved after the first course of treatment a second course results in clinical cure.

In this group of 93 patients 47 were clinically cured, 26 were improved, 16 were not improved and 4 could not be followed up.

In summary it is considered that this bismuth treatment is of value because (1) a large proportion of patients can be cured, (2) desensitization is demonstrated to persist for a long period and hence (3) the worker need not change his occupation or its location. Only if therapy is unsuccessful need there be a change of work.

M. E. Delafield

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

WALTERS, A. H. **The Isolation of Coagulase Positive Staphylococci from Routine Composite Milk Samples.** *J. Applied Bact.* 1959, Aug., v. 22, No. 2, 248–52.

Composite milk samples from 24 farms of varying size and type were examined weekly for 9 weeks by inoculation of 1 ml. of milk into 10% salt broth. Broths were subcultured after 24 hours to blood agar plates from which, after incubation, suitable colonies were picked for the coagulase test. Coagulase-positive strains were tested for their antibiotic sensitivity.

The keeping quality of samples tested was good and the bacterial counts were usually below 10^3/ml.; of the 208 samples examined 127 (16%) contained coagulase-positive staphylococci. The isolation rate in the individual farms over the 9 weeks varied from 11% to 88% but samples from individual farms yielded an irregular number of strains over the period; it was not possible to link high isolation rates with the incidence of herd mastitis. Penicillin-resistant strains were recovered from 10% of samples.

M. Patricia Jevons

MADSHUS, K. & BAARLI, J. **Radiocaesium and Potassium-40 in Norwegian-Produced Milk.** *Nature.* 1960, May 14, v. 186, 527–9, 2 figs.

This work was undertaken to get reliable information about the concentration of caesium 137 in Norwegian produced milk. This radioactive element, with ^{90}Sr; represents the major part of the radiation hazard to man caused by nuclear explosions. It has previously been shown that the northern hemisphere receives the highest fall-out. Further it is known that the ratio Sr/Cs from atomic debris is nearly constant. The qualitative measurement is easier for Cs than for Sr and is detailed herewith. Radioactive potassium is also present in milk and this is allowed for in the measurements. Samples of dried milk were of 250 gm. and the gamma ray activity was measured by means of a scintillation detector. The radioactivity data are charted with rainfall over the whole period of about one year and they give clear indications of association. Seasonal variations are however more clear-cut; during the spring there is a slow increase up to June where an increase of nearly a factor of 2 is recorded. From October onwards there is a general tendency to decrease till January; these changes are attributable only to the feeding conditions. The authors' conclusions are that the content of caesium 137 has increased considerably during the past year and a half. These important measurements are being continued in order to see whether a maximum has yet been reached; there have been no test explosions for about a year, at the time of writing.

S. Russ

JENSEN, P. G. **Caesium-137 in Spray-Dried Danish Milk.** [Correspondence.] *Nature.* 1960, May 14, v. 186, 562–3, 3 figs.

The caesium 137 content of Danish spray-dried milk has been measured in 50 samples, ranging in production time from 1949–59. Scintillation spectroscopy was the method

used and absolute values of content were obtained after deduction of the potassium activity. The peak value obtained up to 1959 was about 20 $\mu\mu$c. caesium-137/gm. potassium. This value is rather lower than in data given by ANDERSON *et al.* (*LASL* Report in *LA*-2296, April 1959) whose work also referred to Danish milk. It is also lower than that of MAYNEORD *et al.* (*Nature*, 1958, v. 182, 1473).

In commenting upon the lowness of his figures the author is inclined to think that it is due partly to the large amount of fertilizer used in Denmark, although exactly how this would lead to a reduction in the caesium is not stated.

From this paper and others cited in the text it evident that a reliable method of checking the dange due to atomic fall-out is coming into general use. Giv the right instruments the procedure seems comparative simple and speedy. *S. Russ*

MCGILLIVRAY, W. A.; PORTER, J. W. G. **Reviews the Progress of Dairy Science. Section I Nutritive Value of Milk and Milk Product Part I** [MCGILLIVRAY]. *J. Dairy Res.* 1960, Jun v. 27, No. 2, 309–21. [135 refs.] **Part 2** [PORTER *Ibid.*, 321–34. [154 refs.]

FOOD POISONING

SHIEL, J. B. **Two Related Food Poisoning Episodes.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1960, Apr., v. 18, No. 2, 24–5.

In August 1958, 48 of 55 guests and staff of an hotel in Scotland were taken ill with sickness and vomiting. An almost pure culture of coagulase-positive staphylococci was isolated from milk stored in a 10-gallon can in the kitchen; cups and jugs were dipped into the supply.

The milk was delivered twice daily from a herd of 18 Jersey cows. All the cows were found to have mastitis, mostly sub-clinical; they had been treated with penicillin or chloramphenicol without veterinary supervision. This milk supply was stopped and there were no further cases.

Coagulase-positive staphylococci were also found in samples of milk from neighbouring farms, in small to moderate numbers.

There is no record of phage typing for this incident.

At the same time a staphylococcal outbreak in a hospital in Southern England was traced to farm cheese made in May 1958 from milk obtained from the same area as that involved in the previous incident. Coagulase-positive staphylococci were isolated from cheese remaining on the farm, from milk and from 2 dairy workers, but the phage types differed from that of the strain isolated from the cheese causing the outbreak, which was 53/54/75. Most of the cows concerned were suffering from sub-clinical staphylococcal mastitis.

It was concluded that there ought to be adequate measures to cool milk and to ensure rapid delivery to the consumer or pasteurization plant. It is stated that milk should not be cooled before cheese making and that therefore the control of milk production is important.

Field studies are advocated on the potential sources and reservoirs of staphylococci, including dairy workers. [A recommendation for the use of only pasteurized milk for cheese making would be helpful.]

Betty C. Hobbs

PIRÉ, E. Su un episodio di tossinfezione alimentare da *S. enteritidis.* [**An Outbreak of Food Poisoning due to** *Salmonella enteritidis*] *Riv. Istituto Sieroterap. Ital.* 1960, Jan.–Feb., v. 35, No. 1, 77–80. [10 refs.]

" A report of a food poisoning outbreak due to *S. e teritidis* occurred in Bari in October 1959, involving individuals. The source of the outbreak was found to horse meat contaminated with *S. enteritidis.*"

FLEMING, R. H. C. **Report on Four Cases of Botulis in Gatooma, S. Rhodesia.** *Central African J. Med.* 1960, Mar., v. 6, No. 3, 91–4.

A mother and 3 children who ate cottage pie at a me shared, except for the pie, with the father and a frien showed symptoms resembling botulism from 1–4 da later; the " cook boy " also showed mild symptoms.

The mother was most severely affected and her illne commenced with nausea and vomiting 24 hours after th meal; the 8-year-old boy started abdominal pains 2 hours after eating the pie, a 5-year-old boy complaine about his eyes and difficulty in swallowing after 4 day and the youngest boy aged 3 showed dilated pupils an a dry tongue and mouth only after 4–5 days. The reached hospital on the 5th day and 5–10% dextrose i normal saline was given intravenously to those wh could not swallow; antitoxin on the 6th day was give to 3 patients and a fourth patient was removed to anothe hospital and put in a respirator.

The progressive symptoms and treatments are given i detail.

4 persons recovered, their conditions improved on th 8th day, but there is no further reference to the child i the respirator.

Clostridium botulinum type B was isolated from bone from the meat used for the pie mixed with substances i contact with the bones, and also from faeces obtaine from the 5 patients. Filtrates from the cultures kille guineapigs unless the animals were protected with ant toxin. *Betty C. Hobbs*

HECKLEY, R. J., HILDEBRAND, G. J. & LEMANNA, C. **O the Size of the Toxic Particle passing th Intestinal Barrier in Botulism.** *J. Exper. Med* 1960, June 1, v. 111, No. 6, 745–59, 8 figs. [13 refs.

HELFRICH, P. & BANNER, A. H. **Hallucinatory Mullet Poisoning. A Preliminary Report.** *J. Trop. Med. & Hyg.* 1960, Apr., v. 63, No. 4, 86–9. [25 refs.]

This is a general account of a type of mild intoxication differing from those previously described, which has been reported in Hawaii in people who have eaten certain mullet (Mugilidae) and surmullet or goatfish (Mullidae) from restricted localities.

There were symptoms of dizziness, loss of equilibrium, lack of co-ordination, hallucinations and mental depression from 10 minutes to 2 hours after eating the fish; there may be nightmares, itching or burning of the throat, muscular weakness and even partial paralysis. Gastro-intestinal upsets rarely occur. Symptoms usually last for a few hours up to 24 hours.

Specimens of the suspected fish including viscera and brain were eaten without ill effect by volunteers investigating the poisoning. Cats and mongooses were fed on the fish also without detectable ill effect.

It is most commonly stated that the fish become toxic through eating the blue-green alga, *Lyngbya majuscula* Gomont, which is abundant in the summer months in the toxic areas. *Betty C. Hobbs*

SAPEIKA, N., UYS, C. J. & MCKENZIE, D. **The Cape Death Cup** *(Amanita capensis).* **An Experimental Investigation.** *South African J. Lab. & Clin. Med.* 1960, Mar., v. 6, No. 1, 12–20, 2 figs. [10 refs.]

Since 1947 at least 12 persons have been taken ill after eating a new species of poisonous fungus *Amanita capensis*, closely related to *A. phalloides*, in South Africa; there were 2 deaths. Vomiting, diarrhoea and other symptoms including cramps occurred 2 hours after eating the fungus. The symptoms resembled those for *A. phalloides*. Experiments with rats showed that very small amounts of extract caused death by injection, yet larger amounts were non-toxic by mouth. It was thought that the active phytotoxins were not readily absorbed from the intestinal tract.

Histological changes in the liver and kidney, and the effect on the ascorbic acid concentration in the liver and adrenal gland were studied in the rat. Toxicity and serum transaminase levels were studied in rabbits.

Betty C. Hobbs

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

VITÉZ, I. Nährböden zur Züchtung und Identifizierung von pathogenen Pilzen. [**Media for Cultivation and Identification of Pathogenic Fungi**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 523–30. [12 refs.]

The English summary appended to the paper is as follows:—

"Five different nutrient media suitable for mycological investigations were prepared. Two media, the one semi-synthetic, the other containing natural ingredients only, served for the isolation of the fungi from test-material. Both the Schizomycetes and the Eumycetes grow well on the two different media.

"The 3 additional nutrients (malt, corn and potato media) served for the identification of fungi. New methods differing from the former, were designed for their preparation. In the media prepared with the new techniques no spontaneous turbidity occurs which is a great advantage for their practical application."

PALDROK, H. **Medical Mycology in Scandinavia and Finland during a Century, from 1841 to 1940.** *Mycopathologia.* The Hague. 1960, May 25, v. 12, No. 4, 289–348. [Numerous refs.]

TULCINSKY-GOLDSTEIN, S. [**Ringworm Infection, its Incidence and Treatment**] *Harefuah.* Jerusalem. 1960, May 1, v. 58, No. 9, [in Hebrew 289–91. English summary 291].

The English summary appended to the paper is as follows:—

"This survey deals with results of treatment of ringworm in infected children and their mothers for the last 6 years. The number of infected patients in 5 maabaroth in the vicinity of Tel-Aviv dropped from a total of 771 in 1953 to 180 in 1959. At the same time the percentage of infected mothers increased from 4% to 22%. The role of the infected mother in spreading the infection in her family is an important one: 66% of all the infected children that are now under our observation have infected mothers. 94% of the children of infected mothers have been found infected during the period surveyed, as compared with 47% of children in infected families with healthy mothers.

"Among 67 X-rayed children of infected mothers 36, mostly girls, who were at the time of treatment below the age of 10 years were reinfected. Children of healthy mothers usually were infected at the age of 6–10—of

infected mothers mostly before the age of 6. The percentage of infected girls is slightly higher than of infected boys.

"There is no spontaneous cure with adolescence.

"Experience showed that X-ray does not stop the epidemic, because most mothers do not accept a treatment which involves head shaving; (b) in cases of reinfection re-X-raying is not recommended.

"The treatment by potassium iodide although time-consuming, is efficient, inexpensive and causes no ill effects, if applied under medical supervision."

PROCHACKI, H. & BIEŁUNSKA, Sabina. Epidemia grzybicy strzygącej głebokiej. [**An Epidemic of Trichophytiasis Profunda**] *Przegląd Epidemiol.* Warsaw. 1959, v. 13, No. 4, 361–9, 5 figs. [20 refs.] English summary.

After the last war sporadic cases of trichophytiasis profunda were observed in the province of Szczecin, Poland, but in 1956–57 the number of cases among the rural population attained epidemic proportions. Micrological investigations showed that the outbreak was due to *Trichophyton mentagrophytes* var. *gypseum granulosum* and *T.m.* var. *g. asteroides*. In 1956, 46 cases were treated in the Dermatological Clinic in Szczecin; the main incidence was between January and May. In 1957, 41 cases were observed. Men and children were mainly affected (40 and 32 cases in the 2 years respectively). The infection was apparently derived from domestic animals. The chin, neck and head were mainly affected, and only rarely the hands. All patients gave a positive response to a skin test with trichophytin. The condition responded to the local application of 90% phenol and 10% glycerol, and desensitization by repeated injections of trichophytin.

D. J. Bauer

SEALE, E. R. & RICHARDSON, J. B. **Trichophyton Tonsurans. A Follow-Up of Treated and Untreated Cases.** *Arch. Dermat.* 1960, Jan., v. 81, No. 1, 87–91, 2 figs. [10 refs.] Discussion 91–4.

The necessity for obtaining further information concerning this insidious form of trichophytosis which has spread in southern areas of the United States to an alarming degree stimulated the authors to undertake the investigations which they record in this article.

101 patients were studied, of whom 84 were under the age of 13 years, 6 between 13 and 17 years and 11 adults. The infection was found 5 times more frequently in boys under 18 years than in girls in the same age-group, but the adult patients numbered 10 females and 1 male.

29 of the patients presented with inflammatory lesions of more or less severity, and all had recovered at the time of writing. Only 1 of these was epilated with X-rays. [It was of especial interest that 3 of this group were adults (2 women and 1 man).] The authors express the view that when inflammation is associated with this type of ringworm the course of infection lasts much longer than it does when inflammation is associated with th type of infection due to species of *Microsporum*.

As regards the non-inflammatory group, 52 were epi lated with X-rays while the other 21 were treated wit topical fungicides or were not treated at all.

Of 46 children treated with X-rays, 39 were free o infection after 5 months, while 7 were failures; but whe 3 of these were subjected to X-ray therapy for the secon time they recovered after periods varying from 2, 3 an 18 months respectively. The other 4 remained infecte for several years afterwards.

Treatment of adult patients with X-rays produce varied results, whereas those treated with various topica applications did not respond at all.

The authors conclude that females are less resistant t infection than males, that some degree of inflammator response favours the course of the disease, and lastly topical treatments are ineffective. *C. J. La Touche*

RODRÍGUEZ, M. A. & GONZÁLEZ BENAVIDES, J. Tinea Nigra Palmaris en México. Aislamiento de *Cladosporium werneckii* en el Estado de Nuevo León. [**Tinea Nigra Palmaris in Mexico. Isolation o *Cladosporium werneckii* in the State of Nuevo León**] *Rev. Latinoamer. Microbiol.* Mexico. 1959 Dec., v. 2, No. 4, 199–205, 4 figs. [12 refs.]

The English summary appended to the paper is a follows:—

"One case of tinea negri palmaris is reported. Th lesion had its site in the palm of the left hand. The diag nosis was established by the clinical picture and by direc examination of scrapings obtained from the lesion i KOH and Schiff-periodic technic. Typical colonies o *Cladosporium werneckii* were obtained by culture. Th case is the second we have known of in Mexico. Con sidering the biogeographical and climatological character istics of the country it is surprising that only these case have been brought to our attention. It is believed tha this is due to failure to recognize the lesion, or that it i readily confused with nevi or that due to its mild clinica picture the patient does not seek medical advice."

CHAVES, A. R. & ABRANCHES, P. A griseofulvina no tratamento das tinhas do couro cabeludo (ensaio clínico). [**Griseofulvin in the Treatment of Ringworm of the Hairy Skin**] *Gaz. Méd. Portuguesa* 1959, Nov.–Dec., v. 12, No. 6, 667–76. [17 refs.] English summary.

The authors report that results obtained in treating cases of tinea tonsurans in children aged between 1 months and 12 years by Fulcin tablets containing 25 mgm. griseofulvin. 4 were due to *Microsporum canis*; to *M. audouini*; 1 to *Trichophyton violaceum*; 2 to *T tonsurans*. The dosage was from 0·5 to 1 gm. dail depending on body weight, divided into 3 or 4 doses. N local treatment except washing the hair well with soa and water was advised. The drug was well tolerated an side effects (temporary dizziness) occurred in 1 case only

treatment lasted between 37 and 52 days and all but 1 were cured on the first course, the patient who relapsed was cured by a second course.

The authors consider that because of its efficacy and ease of application this treatment has enormous advantages; it should however be continued for some days after apparent cure and auto-infection avoided by thorough washing of the hair. *W. K. Dunscombe*

MACKINNON, J. E. & CONTI-DÍAZ, I. A. Miositis en la histoplasmosis experimental. [**Myositis in Experimental Histoplasmosis**] *An. Facul. de Med. Montevideo.* 1959, v. 44, Nos. 5/6, 608–9.

The English summary appended to the paper is as follows:—

"Five mice were inoculated intravenously with the yeast-like form of *Histoplasma capsulatum*. Besides the classic visceral and lymphatic lesions we observed in 2 animals the invasion of the diaphragm, the myocardium and of the tongue and in 1 animal also of the skeletal muscles. The epithelium of the tongue was ulcerated in one animal."

STOUGH, A. R., GROEL, J. T. & KROEGER, W. H. **Amphotericin B, a new Antifungal Agent for the Prophylaxis of Antibiotic-Induced Moniliasis.** *Antibiotic Med.* New York. 1959, Nov., v. 6, No. 11, 653–61. [33 refs.]

In antibiotic-induced moniliasis it is generally conceded that the main factor in the development of infection is the alteration in the microbial flora. It is also conceded that the broad-spectrum antibiotics are mainly responsible for bringing this about.

Nystatin combined with tetracycline has been in use as a prophylactic, but the authors of this article consider that there are some unfavourable features associated with this combination. These are chiefly: the limited aqueous stability of tetracycline-nystatin liquid preparations, the unacceptability of this combination in an oil vehicle to some patients, and in the view of some clinicians the danger of aspiration. Moreover, its bitter taste is repugnant.

Amphotericin B has been found to be more active against species of *Candida*, is more stable in aqueous medium than is nystatin and does not possess a bitter taste. However, like nystatin it is poorly absorbed from the gastro-intestinal tract [which is perhaps in its favour since it is said to possess toxic properties].

The authors set themselves the task of confirming the reputed ability of amphotericin B to limit or depress the overgrowth of *Candida albicans* induced by tetracycline therapy and of ascertaining the possible influence of amphotericin B on the absorption by the gastro-intestinal tract of concomittantly administered tetracycline. 118 healthy adults received therapeutic doses of tetracycline for 1 week before the combined therapy. Various tests were made on these subjects and it was found that the best tetracycline:amphotericin ratio was 5:1, which reduced the average stool content of *C. albicans* by 93% after 7 days.

In tests for the amount of absorption of tetracycline and amphotericin from the gastro-intestinal tract 20 subjects received therapeutic doses of the combined drug. Serum specimens taken subsequently at intervals and assayed against the appropriate organisms showed that there was good absorption of tetracycline but no appreciable absorption of amphotericin B.

C. J. La Touche

DROUHET, E., HIRTH, L. & LEBEURIER, G., with the technical collaboration of Huguette BOVE. Mode d'action des antibiotiques antifongiques. I. Action de l'amphotéricine B sur le métabolisme respiratoire de *Candida albicans*. [**Mechanism of Action of Antifungal Antibiotics. I. The Action of Amphotericin B on Respiratory Metabolism of *Candida albicans***] *Ann. Inst. Pasteur.* 1960, Apr., v. 98, No. 4, 469–84, 10 figs. [25 refs.]

Amphotericin B in concentrations as high as 50 μgm./ml. provokes an increase in oxygen uptake in suspensions of *Candida albicans* in both the presence and absence of glucose at *p*H 7·0. At *p*H 4·2 this increase is only caused by a much lower concentration (1·56 μgm./ml.) and higher ones cause a decrease. A decrease also results when the cells are washed after contact with the antibiotic. In an atmosphere of nitrogen, the antibiotic stimulates CO_2 production either in the presence or absence of glucose. It is suggested that amphotericin B may have an action similar to that of agents which uncouple phosphorylation: the hyperthermia which can be caused by 2,4-dinitrophenol results from the stimulation of cellular oxidation such as appears to be revealed in these experiments. *L. P. Garrod*

FORBUS, W. D., FUKUNAGA, N., VAN SCHOOTE, A. & CRESS, Hertha. **Reaction of Chorioallantoic Membrane of Chick Embryo to *Nocardia intracellularis* Inoculation.** *Arch. Pathology.* 1960, May, v. 69, No. 5, 571–7, 3 figs. [15 refs.]

MURESAN, A. **A Case of Cerebral Mucormycosis diagnosed in Life, with Eventual Recovery.** *J. Clin. Path.* 1960, Jan., v. 13, No. 1, 34–6, 4 figs. [15 refs.]

This description of a case of cerebral mucormycosis in Rumania adds yet another record of this usually fatal disease to a list which has been increasing steadily, especially during the past decade [see also this *Bulletin*, 1960, v. 35, 125].

The patient concerned was a male aged 18 years. He had been recently "suffering from headache, giddiness, and vomiting for about 3 weeks." On examination, he was found to be slightly pyrexial, and presented with signs of central nervous system disease. Subsequently, operation revealed the presence of an intracerebral cyst containing turbid reddish material. This was excised. The post-operative course was uneventful, and the patient was able to resume his occupation.

Histological examination of the cystic biopsy specimen revealed patches of granulation tissue within its cavity containing "sparse calcosphaerites." Numerous non-septate hyphae were associated with this tissue, especially in the neighbourhood of the blood-vessel walls which they tended to invade. Many of the hyphae had unde gone calcification.

Unfortunately no cultures were made to confirm th diagnosis, but the authors were satisfied that the aeti logical agent was a member of the *Mucoraceae*

C. J. La Touche

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

LARSSON, J. & LINELL, F. Tuberkulos och mortalitet. [**Tuberculosis and Mortality**] *Svenska Läkartidningen.* 1960, May 27, v. 57, No. 22, 1703–7.

A table gives the official number of deaths from all forms of tuberculosis in Sweden in different years. In 1954, for example, there were 935 such deaths. In 1955 they were down to 775, and in 1958 they were further down to 511. It is argued that these figures, however inducive of self-complacency, err grossly by understatement, witness the following observations:— At the Malmö general hospital 2,972 post-mortem examinations were carried out during the 3-year period 1957–59. Among them were 51 cases in which active tuberculosis was found, 45 of the 51 being pulmonary. This gives an incidence of only 1·7%, but on further scrutiny of the 51 cases it was noted that in less than half of them, only 23, had the disease been recognized clinically. In the remaining 28 cases, 22 of which were pulmonary, it had been left to the pathologists to discover active, florid tuberculosis.

It was also disconcertingly instructive to note the ages of these tuberculous patients classified according as their tuberculosis had or had not been diagnosed before death. The mean age of those whose tuberculosis had been diagnosed in their lifetime was 57 years, whereas it was 74 for those whose tuberculosis had been overlooked while they lived. Many of them had had ailments obscuring their tuberculosis—cardiac infarct, arteriosclerosis, encephalomalacia, arthritis, pyelonephritis and (in 6 cases) cancer. Yet among these missed cases of tuberculosis there were as many as 15 in which pulmonary tuberculosis had been the main illness. If these Malmö figures are applied to the whole of Sweden, it would be closer to the mark if the above-mentioned 511 deaths from tuberculosis in 1958 were doubled.

Claude Lillingston

HORWITZ, O. **Lupus Vulgaris Cutis in Denmark 1895–1954. Its Relation to the Epidemiology o Other Forms of Tuberculosis. Epidemiology and Course of the Tuberculous Infection, based on 3902 Cases from the Finsen Institute Copenhagen.** *Acta Tuberculosea Scandinavica* 1960. Suppl. 49. 142 pp., 36 figs. [Numerou refs.]

WORLD HEALTH ORGANIZATION. **Tuberculosis Survey i Nigeria.** 25 mimeographed pp., 3 figs. 1957, Dec Copenhagen: W.H.O., Tuberculosis Research Office

This survey was made in Nigeria (population 31· million (1957)) in 1955 and 1956 under the direction o the WHO Regional Office for Africa. It consisted in th examination of a sample of the population by tuberculi testing and the bacteriological examination of sputum.

The communities were selected by region so as to in clude a variety of geographical situations. 15 communi ties were examined, the last 3 in the series being randoml selected. The samples reflected fairly the age and se composition of the general population of the country The total number of persons included in the survey wa 9,291.

Sputum was collected from 4,956 (94·9%) of the 5,22 persons in the sample who were over 12 years old. 1 sputa (0·26%) were found to contain acid-fast bacilli o direct examination. Variations in incidence from localit to locality were small. In another 13 specimens a fe particles were observed which could have been eithe atypical acid-fast bacilli or artefacts.

11 of the 13 positive sputa were cultured on Löwen stein-Jensen medium, and 6 yielded a growth. These wer the only positive cultures obtained from 2,502 specimens 210 strains of atypical acid-fast bacilli were isolate

which were not tubercle bacilli of human, bovine or avian type. 75% came from a single village where 22% of all the sputa collected yielded cultures of atypical mycobacteria.

A Mantoux test with 5 TU of PPD was given to all participants. Owing to the large number of reactions of medium size it was not possible to distinguish clearly between those who had been infected by the tubercle bacillus and others. There was evidence of non-specific tuberculin sensitivity due to organisms other than human or bovine mycobacteria.

Estimates were made of the percentage of persons infected with the tubercle bacillus at different ages: 0–4 years, 6·6; 5–9, 25·3; 10–14, 42·6; 15–19, 56·6; 20–29, 79·5% and over 30, 88·0%. The overall rate of infection was estimated to be 57·4%. *H. G. Calwell*

World Health Organization. **Tuberculosis Survey in Ibadan, Nigeria. September 1957–January 1958.** 18 mimeographed pp., 3 figs. 1958, May. Copenhagen: W.H.O., Tuberculosis Research Office.

The West African Tuberculosis Survey Team of WHO carried out a survey in Ibadan, Western Nigeria (population in 1957, 336,000) in 1957–1958. The part of the town being surveyed was divided into 2,000 random sample units, a number of which were further selected also at random, 2,298 persons were included in the sample, less than 1% of the African population of the town. Males and females were about equal in numbers except in the age-group 20–29 years in which there was a high proportion of females.

Out of 1,975 persons eligible for the Mantoux test (5 TU of PPD) 1,606 (81·3%) completed it. The test was not very efficient in separating the samples into an infected and an uninfected group because of the high frequency of intermediate-sized reactions thought to be due to non-specific mycobacteria.

It was estimated (with caution, the authors state) that over 50% of children aged 10–14 and over 70% of persons aged 15–19 had been infected by the tubercle bacillus.

Sputum was collected from persons over the age of 10 years, stained by the Ziehl-Neelsen method and examined for acid-fast bacilli. Some positive sputa were sent to Copenhagen for culture.

1,594 (95·9%) of the 1,663 persons eligible for sputum examination provided sputum. Acid-fast bacilli were found in 10 (0·6%). The prevalence of such infectors in the population was estimated to be between 0·3% and 1·2%. *H. G. Calwell*

World Health Organization. **Tuberculosis Surveys in Ghana. January–August 1957.** 27 mimeographed pp., 4 figs. 1958, May. Copenhagen: W.H.O., Tuberculosis Research Office.

3 tuberculosis surveys were made in Ghana (population 4,836,000) in 1957. Samples were selected at random from the total African population, from 2 urban areas and from an industrial group (gold-mine workers). The methods used were testing with tuberculine and microscopic examination of sputum.

The samples examined comprised 2,919 persons of the general population, 688 of the urban group and 394 of the industrial group.

The Mantoux test with 5 TU of PPD was used. It was completed in 87% of the general group and 82% of the urban group. A specimen of sputum was collected from each person whose age was estimated to be 13 years or over. Sputa found to be positive for acid-fast bacilli on direct examination were sent to Copenhagen for bacteriological examination by culture; in addition 25% of negative sputa were sent also.

In no age-group was the Mantoux test with 5 TU very effective in dividing the population into infected and uninfected groups. This was due to the presence of non-specific sensitivity, the incidence of which varied in different regions.

On the assumption that induration of 10 mm. or more indicated tuberculous infection it was estimated that in the general population the percentages infected were: 0–4 years, 6·2; 10–14, 35·7; 20–29, 66·9% and over 40 84·5%. The rates in the urban group were 6·0, 43·3, 78·4 and 92·3 respectively.

8 persons (0·5%) in the general group, 2 (0·5%) in the urban group and 5 (1·3%) in the industrial group were found to have acid-fast bacilli in their sputum. The presence of tubercle bacilli was confirmed by culture in 7 of the 15 specimens. The number of persons excreting acid-fast bacilli was estimated to lie between 0·2% and 0·9% in the general population, between 0·1% and 1·8% in the urban population and between 0·4% and 3·0% among the underground gold-mine workers.

H. G. Calwell

Ingham, F. J. **Control of Pulmonary Tuberculosis in the Brigade of Gurkhas in Malaya, 1955 to 1958.** *J. Roy. Army Med. Corps.* 1960, Apr., v. 106, No. 2, 68–81.

Lack of knowledge about the epidemiology of tuberculosis in Nepal contributes to the incompleteness of control of the disease in the Gurkha soldiers from that country who serve in the British Army in Malaya.

The hospital admission rate for pulmonary tuberculosis for the period 1948–1957 averaged 7·1 per 1,000 men yearly, which was nearly 10 times the rate for British soldiers serving in Malaya.

The tuberculin reactor rate in recruits showed that tuberculous infection was fairly evenly distributed throughout the various areas of Nepal from which the soldiers came but there was evidence that there could be small isolated areas still untouched by tuberculosis. The total reactor rate in 5,676 recruits tested in 1951–1957 was 62·1%. There is a sharp rise in conversion rates during the first 9 years of service with slowing down thereafter. The total rate after 18 years is 100%. Most of the patients (73·1%) were admitted in the first 10 years of service; 37·9% in the 5th–10th years.

The control scheme includes X-ray examination on entry and routine re-examination, tuberculin testing and BCG vaccination, notification of cases, treatment and

follow-up. The soldiers' families are cared for in the same way.

In 1957–1958 9,773 soldiers and 4,029 members of families were examined by X-ray. The incidence of tuberculosis was found to be 4·05 and 0·87 per 1,000 respectively. The incidence in other Commonwealth troops was 1·2 and in locally employed civillians it was 9·8.

Likely sources of infection include the civil population encountered on the journey between Nepal and Malaya. In addition the soldiers have undergone the strain of jungle warfare for a long time.

Early notification of active tuberculosis is the rule; contacts are traced and examined by X-ray, tuberculin tested and if suitable vaccinated with BCG. [See also this *Bulletin,* 1948, v. 23, 93; 1956, v. 31, 1,092.]

H. G. Calwell

MIHOV, H. La Tuberculose d'Inoculation chez les enfants. **[Inoculation Tuberculosis in Children]** *Folia Med.* Plovdiv. 1959, v. 1, No. 2, 81–5. [14 refs.] [In Bulgarian.] French summary.

The following is a translation of the author's summary in French:—

The author presents a clinical and epidemiological study of 152 cases of inoculation tuberculosis, which occurred in 5 epidemics. He has himself observed 89 cases, and this large number has enabled him to describe the clinical picture and epidemiology, and to make certain important theoretical deductions.

Inoculation tuberculosis is iatrogenic in that it results from medical procedures, and it affects only subjects previously uninfected with tubercule bacilli, largely children. Observations and epidemiological studies prove the exogenous origin of the infection, which may occur sporadically or in the form of an epidemic. In sporadic cases the infection is conveyed by a syringe which has been badly sterilized or has been contaminated. Epidemics occur when infective material is aspirated from a tuberculous abscess, and the syringe is then used for serial injections in healthy subjects.

Clinical observations show that the early toxic signs precede the appearance of allergy by several weeks, and this indicates a distinction between the incubation period and the pre-allergic period, which at present are regarded as the same. The presence of a classical primary complex, with its primary focus and regional lymphadenitis, in every case of inoculation tuberculosis does not uphold the view that primary complex need not occur ("incomplete complex"). In all the subjects examined the primary lesions were found at the site of injections, and never elsewhere; this fact does not support the view that the primary focus may be independent of the site of entry.

Charles Wilcocks

STEIN, S. C. & HETHERINGTON, H. W. **Fifteen Years' Experience with the Tuberculin Test.** *J. Amer. Med. Ass.* 1960, May 14, v. 173, No. 2, 129–35. [10 refs.]

In the authors' opinion the Mantoux test is the most reliable of the tuberculin tests; it permits accurate recording of the degree of sensitivity present in differe patients or in the same patient at different times.

Old Tuberculin (OT) cannot be standardized ad quately but purified protein derivative (PPD) of tube culin produced from a culture on a synthetic medium ca be standardized. The authors give a useful account the various dosages of OT and PPD in use and the equivalents in International Units (TU).

During the period 1941–1955, 22,014 patients attende a chest clinic in the U.S.A. The majority suffered fro tuberculosis or were contacts of tuberculous patients bu some had non-tuberculous respiratory and other disease After excluding a certain number for reasons stated th results of Mantoux testing with PPD were analysed fo 19,235 patients.

The total reactor rate to the 1st dose of PPD (0·0000 mgm.) was 65·2% and to the 2nd dose (0·005 mgm 19·2%, total 84·4%; 4·8% did not react to the 1st dos and failed to complete the test with the 2nd. Both test were negative in 10·7%.

23·9% of the reactors to the 1st dose and 3·7% of th reactors to the 2nd dose had pulmonary tuberculosis 40 (1·9%) of the 2,054 patients who were negative to bot tests had pulmonary tuberculosis.

The results of the tests were analysed in 3,215 patient with pulmonary tuberculosis: 93·5% reacted to the 1s and 4·3% to the 2nd dose; 1·2% were negative to both

It was shown that the degree of sensitivity to tuber culin yields important information. In the selected pop ulation there was a higher incidence of disease in thos with marked sensitivity than in those with lower degree of sensitivity. There was however no evidence that th extent of pulmonary disease present was the factor tha determines the intensity of the tuberculin reaction.

The authors conclude that the standard 2-dose test i satisfactory and should not be modified in clinics tha serve areas where tuberculosis is still a major publi health problem. They advocate the reinstitution o standardization of tuberculin for Mantoux testing.

H. G. Calwell

ROBINS, A. B. & DALY, Joan N. **Evaluation of the Heaf Tuberculin Test.** *New England J. of Med.* 1960 May 19, v. 262, No. 20, 1008–12, 1 fig.

The New York City Health Department became dis satisfied with the Vollmer patch tuberculin test in th school-health tuberculosis-control programme because i was not sufficiently sensitive or specific. The Mantoux test was also tried but found to be unsatisfactory becaus of difficulty in getting facilities for adequate sterilizatio of instruments and of the amount of time necessary fo its performance.

Trial was therefore made of the Heaf multiple punc ture test with PPD (2 mgm./ml.). In a group of 1,238 high-school students the patch test was positive in 4·4% and the Heaf test in 9·1%. 5 pupils had positive patch and negative Heaf tests whereas in 63 the Heaf test wa positive and the patch negative. Delayed positive Heaf reactions were seen (after 72 hours) in a number of pupils and it was found that the highest number of positive reactions was reached at 7–8 days.

The Heaf test was next compared with the Mantoux test (10 TU of OT). 30% of 507 pupils showed positive Heaf reactions, and only 21% reacted to the Mantoux test (induration of 5 mm. or more). In 55 the Heaf test was positive and the Mantoux negative; in only 9 was the Heaf negative and the Mantoux positive. Only 94 students came back for reading at 13 days; 71 who had been recorded as Mantoux negative at 72 hours and only 1 was now positive. 20 of the 63 who showed no Heaf reaction at 72 hours were now classed as positive.

A group of children, many of whom were known reactors and most of whom had been vaccinated with BCG, were given simultaneous Heaf and Mantoux tests with 5 or 250 TU of PPD. More reacted to the Heaf test than to the Mantoux with 5 TU. Most of the difference was due to delayed Heaf reactions. The specificity of the Heaf reaction was demonstrated by the finding that when 250 TU were given, 806 out of 821 (98%) of all persons positive to the Heaf test also reacted to the Mantoux test in one of the dosages used.

The degrees of reactions to the Heaf and the Mantoux tests with 5 TU were compared. There were 2 groups of subjects, *viz.* one of young persons under 18 years of age and the other of patients in a chronic-disease hospital most of whom were over 70 years of age. The Mantoux tests were read at 72 hours and the Heaf at 7 days. Out of a total of 1023 subjects 451 (44%) reacted to the Heaf test and 236 (23%) to the Mantoux; 109 of the Heaf reactions were classed as weak and all but 3 of these occurred in Mantoux negative persons. 43 of the 139 with strong Heaf reactions were also Mantoux positive. These results led to the conclusion that weak positive reactions to the Heaf test should be disregarded in mass tuberculin surveys.

In the authors' opinion the Heaf test is a satisfactory substitute for the Mantoux test in mass surveys. [This reviewer could have followed the comparison of degrees of reactions better if the authors had used Heaf's criteria of positive reactions rather than their own.]

H. G. Calwell

ROCHESTER, W. R. **The Convenience of the Heaf Method for Tuberculin Testing.** *Central African J. of Med.* 1960, Apr., v. 6, No. 4, 141–3, 1 fig.

20,000 African schoolchildren in Southern Rhodesia were tested in 1958 with the Heaf gun, with undiluted Old Tuberculin; the needles were set at 2 mm. penetration. The tests were read usually on the 4th day and occasionally on the 5th day.

Some results are given:

Unvaccinated Schools

Standard	Total Read	Positive	Reactor Rate %
A (average age 7 years)	2,737	707	26
B	2,294	761	33
I	1,767	619	35
II	1,201	485	40
III (average age 13 years)... ...	900	408	45

Schools in which BCG Vaccination had been done in 1954

Standard	Total Read	Positive	Reactor Rate %
A	852	247	29
B	707	264	37
I	591	314	53
II	453	294	65
III	325	249	77

[No information is given about the amount of vaccination that had been done in the schools but judging by the disparity in reactor rates in the older children in the 2 series many must have been vaccinated.]

The Heaf test was found very convenient to perform. The use of undiluted tuberculin, which has a long life, is an added recommendation to those working in tropical countries. *H. G. Calwell*

SARTWELL, P. E. & DYKE, L. M. **Comparative Sensitivity of College Students to Tuberculins PPD-S and PPD-B.** *Amer. J. Hyg.* 1960, Mar., v. 71, No. 2, 204–11, 1 fig.

This work was done in the State of Maryland, U.S.A. The authors' aim was to compare the frequency of reactions to standard PPD (PPD-S) and a tuberculin prepared from the Battey bacillus (PPD-B) in college students. The tests were done by intracutaneous injection and read at 48 hours. The criterion of a positive reaction was induration of 5 mm. or more. The dose was 0·1 ml. of a strength of 0·001 mgm./ml. which corresponded to 5 TU of PPD-S. Details of the random distribution of the students and the performance and reading of the tests are given and of the precautions taken to exclude bias.

There were 783 male students of mean age 18·6 years and 442 females of mean age 18·5 years. Examination of the size of the reactions showed that the distribution for PPD-S was bimodal while the frequency of those to PPD-B declined steadily with their size.

7·6% reacted to PPD-S and 23·0% to PPD-B. A significantly larger proportion of males than of females reacted to PPD-B but the difference by sexes in reactions to PPD-S was smaller and not statistically significant.

The reactions of students who had lived their whole lives in a single community were analysed. The reactor rate to PPD-S was twice as high in the residents of the 2 large cities in the State as in the others.

Of the 26 students who gave a history of family contact with tuberculosis 13 (36%) reacted to PPD-S and 15 (42%) to PPD-B. These rates are much higher than those in non-contacts. The reactions to PPD-S measured 0–1 mm. in 23 contacts and were over 14 mm. in the other 13. These 13 all had larger reactions to PPD-S than to PPD-B.

Examination of correlation between reactions to these tuberculins provided a suggestion that reactors to either may include 2 kinds of individuals *viz.* those who do not and those who do cross-react to the second antigen. It is possible that sensitivity to PPD-B is a result of sensitization by any one of several antigens with different capacities to cross-sensitize to PPD-S. The higher reactor rate to PPD-B in males than in females is not explained. [See also this *Bulletin*, 1959, v. 34, 208.] *H. G. Calwell*

GRIEP, W. A. & BLEIKER, M. A. Vergelijking van een Nederlandse met een Deense gezuiverde tuberculine. **[A Dutch and a Danish Purified Tuberculin compared]** *Nederl. Tijdschr. v. Geneesk.* 1960, May 21, v. 104, No. 21, 1025–8.

The English summary appended to the paper is as follows:—

"A purified tuberculin made in Denmark for the international market, PPD Rt 23 (Purified Protein Derivative), was compared with a Dutch product, PPD—Utrecht. These two types of tuberculin are comparable for Mantoux tests done with a dilution of 1 T.U. in 0·1 ml. Tween 80 added to these tuberculin dilutions has a stabilizing effect, as it counteracts the adsorption of tuberculoproteins to the surface of the glass. On the other hand it will reduce the degree of redness and induration in the reactions, which must be taken into account when examining the site of the injection. The number of bullous reactions is reduced considerably by the addition of Tween 80."

GLASS, Dorothea D., GINSBURGH, Fruma W. & BOUCOT, Katherine R. **Screening Procedures for Pulmonary Disease in Prenatal Patients.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 689–94, 2 figs.

Adverse publicity about the danger of radiation caused the authors to undertake a study of the value of confining routine X-ray examination of the chests of women under antenatal supervision to those showing tuberculin sensitivity. The object of the enquiry was to determine the number of women with significant tuberculosis who would be missed by such a procedure.

The Mantoux test was used with 1 and 5 TU of PPD; the criterion of a positive reaction was the presence of induration of at least 5 mm. at 72 hours.

The first group of women consisted of 310 antenatal clinic patients. After 150 had been tested it was seen that about half of the patients had failed to return for readings. The study was then expanded to include all obstetrical ward patients in the authors' hospital, and a similar programme was conducted in the obstetrical wards of another hospital, and in a group of private obstetrical patients.

22% of the antenatal clinic and ward patients reacted to 1 TU and 10% to 5 TU. The total reactor rate of 28% is based on 60 reactors to 1 TU and 23 reactors to 5 TU among 285 clinic patients plus 47 reactors to 1 TU and 11 reactors to 5 TU in 211 ward patients. Owing to the depression of tuberculin sensitivity which is believed to occur during pregnancy these rates may be lower than if the same women had been tested before pregnancy. There was no radiological evidence of significant tuberculosis in any patient.

All but 1 of the tests were read in the group of 153 private patients. The reactor rate was 15%. Of the 621 obstetrical patients tested in another hospital 189 had left before reading. The analysis is based almost entirely on 409 Negro women whose tests were read. The total reactor rate was just over 20%. One case of sarcoidosis was detected in a non-reactor.

The authors conclude that tuberculin testing as a substitute for routine X-ray examination in antenatal clinics is impracticable in large city hospitals. The decision whether or not tuberculin testing may be wisely substituted for routine X-ray examinations should be based on the proportion of tests read, the reactor rate and the proportion of significant chest disease in non-reactors.

H. G. Calwell

GROVE, W. S. & MCNAB, G. R. **Practical Application of Respiratory Function Testing in Chest Hospital Work.** *Tubercle.* 1959, Feb., v. 40, No. 1, 26–43, 6 figs. [Numerous refs.]

The authors point out that many reports are uncritical of the value of respiratory function tests, and they investigate whether function tests provide a measure of the limit beyond which any given surgical collapse procedure is likely to cripple or kill the patient. They set out (1) to measure the effect of collapse and surgical measures on the "values" found by respiratory function testing; (2) to compare these values with the clinical state of the patient before and after such measures; (3) to assess how far such testing might aid decision as to when such measures were justifiable.

They begin by discussing the literature on respiratory function tests in tuberculous patients submitted to collapse and surgical measures, and analysing the results obtained by other workers. They then describe the apparatus and techniques used for respiratory testing in the Foxhall Hospital at Ipswich. They consider that relative values are preferable to absolute in assessing the results of the physiological examinations discussed.

The results are presented of routine testing of respiratory function before and after 167 therapeutic procedures in patients suffering from pulmonary tuberculosis. The results of these tests are then compared with the clinical assessment of the patient. The authors conclude that routine testing is of less value in such cases than is a careful clinical and radiographic assessment in foretelling the effect of mechanical treatment procedures, but on the whole bronchospirometry is more likely to furnish useful information than many other procedures. A table is given showing the initial grading of patients compared with the outcome after treatment, and the comparison is very close.

This paper is difficult to summarize, and should be read in full by those who are interested in this type of work.

F. H. Young

ROTHMAN, P. E., JONES, J. C. & PETERSON, H. G., Jr. **Endoscopic and Surgical Treatment of Pulmonary Tuberculosis in Children.** *J. Dis. Children.* Chicago. 1960, Mar., v. 99, No. 3, 315–28, 5 figs. [34 refs.]

This paper gives a good general account of primary tuberculosis as it affects children with special reference to its effect on the bronchi. This is followed by an account of 3 cases in some detail and a comment. The authors point out that there is no general agreement on the extent of the use of bronchoscopy and surgical resection in these children. They do not think that routine

bronchoscopy is indicated in all cases of primary pulmonary tuberculosis in children. It should be limited to patients with suggestive clinical and radiographic evidence of endobronchial involvement.

Early bronchoscopy may help to establish the diagnosis of active tuberculosis; it may also reveal an unsuspected foreign body or pyogenic infection. Removal of caseous plugs may prevent a rare catastrophe due to suffocation as well as relieve dyspnoea. It may permit an atelectatic lobe to re-expand, relieve obstructive emphysema, and prevent the development of obstructive pneumonitis and bronchiectasis.

The characteristics of the segmental lesion are described, and it is pointed out that the right middle lobe is singularly susceptible. Various authors are quoted showing the difference of opinion that exists as regards the role of surgical resection. CAMERON, *et al.* [this *Bulletin,* 1958, v. 33, 568] reviewed records of 409 children under 16 during 1949–1955. They concluded that only 36 of the more persistent form of segmental lesions deserved consideration because there appeared to be residual lung damage. They conclude that all in this group may require surgery in the future, but in the absence of symptoms the operation was not justified at the present time. TEMPLE (Personal Communication to Authors, 1958) states that he would prefer to allow any tuberculous activity to subside on conservative lines and has seen no case with dissemination of disease while left under medical treatment. He regards 2 years as a safe period which should be allowed to elapse between the original lesion and the operation.

LINCOLN [this *Bulletin,* 1958, v. 33, 650] and her associates, reporting 10 children with endobronchial tuberculosis who had surgical resections, is slightly less conservative than Temple, especially concerning the timing of surgery. Surgery should be considered in patients with extensive areas of bronchiectasis and obviously airless segments. Definite marked narrowing or stenosis of the bronchus should also be an indication for surgical consideration. Similar opinion is reported by HUISH dealing with the resection of segmental lesions in 29 children and adolescents (*Thorax,* 1956, v. 11, 186). Good results are reported but Dillwyn THOMAS's [this *Bulletin,* 1953, v. 28, 171] procedure of opening the gland capsule, curetting the contents, and closing the incision in the capsule is probably a sounder operation than dissecting out a gland, which may be very dangerous.

Decortication for constrictive pleuritis of tuberculous origin is seldom performed in children, and it is thought that the use of adrenal steroids plus antimicrobial therapy will largely prevent the necessity for this. The authors conclude that children require surgery for grossly damaged areas of the lung, especially involving the middle and lower lobes, and for contracted airless segments that often contain caseous residues and are associated with bronchial strictures. They quote with approval the opinion of Cameron and associates that the curative value of an ordered and tranquil life in a children's sanatorium is very valuable, and that it is seldom that results comparable to the series quoted could be obtained in normal home conditions of most of the patients. *F. H. Young*

HEILESEN, B. **Diffuse Goitre induced by PAS.** *Acta Tuberculosea Scandinavica.* 1960, v. 38, Nos. 3/4, 325–31, 3 figs. on 3 pls. [10 refs.]

GROTH-PETERSEN, E., GAD, U. & ØSTERGAARD, F. **Mass Chemoprophylaxis of Tuberculosis. The Acceptability and Untoward Side Effects of Isoniazid in a Control Study in Greenland.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 643–52, 1 fig. [17 refs.]

In 1956 a study of the potential value of isoniazid in preventing tuberculous disease in adults in Greenland was begun [this *Bulletin,* 1957, v. 32, 1042].

Nearly the whole adult population aged 14 years and over participated. As a condition of participating all persons were required to undergo X-ray examination to exclude those already suffering from active tuberculosis; it was known that most adults were tuberculin positive. The 79 villages included were divided into 2 groups, and 1 of every 2 successive villages in each group was assigned at random isoniazid and the other placebo. No one outside the administration of the trial knew what part of the population got isoniazid and what part placebo.

The average dose of isoniazid was 7 or 10 mgm./kgm. daily on 2 successive days weekly. The placebo pills contained 0·1 mgm. of isoniazid and 2 mgm. of quinine to provide a bitter taste resembling isoniazid. Both pills were of the same size, shape, colour and weight. The number of each given was the same. Both the treatment and the control groups were given pills for 2 periods of 13 weeks with an interval of 13 weeks.

There were 5,157 persons in the isoniazid group and 4,955 in the control group; 82·4% and 85·3% respectively completed the course. The total rate of discontinuance was 6·2% in the isoniazid group and 3·5% in the other.

Spontaneous complaints of symptoms were made by about 1% of the participants in each group. All symptoms were slight and were similar in character in both groups. The total frequency of side effects was so low that it was seen that chemoprophylaxis with isoniazid in the above dosage can be carried through without risk in a general population. A final conclusion on the value of the procedure "will have to await an evaluation of the potential harm caused by development of isoniazid-resistant bacilli in the population in comparison with the potential benefit of prophylaxis in reducing tuberculosis morbidity". *H. G. Calwell*

NATVIG, H. Sykelighet og fravaer blant yrkesvalghemmede tuberkulöse i en Oslo-bedrift. [**Morbidity and Absenteeism among Industrially Handicapped Tuberculous Persons in an Oslo Industry**] *Tidsskr. f.d. Norske Laegeforening.* 1960, June 1, v. 80, No. 11, 537–44, 4 figs.

In November 1954 Natvig presented a report on the 119 tuberculous workers who had been employed by an electrical-mechanical industrial concern in Oslo during the 8-year period 1946–53. For the whole of this period the absenteeism of these workers had been 3 times

greater than that of the non-tuberculous, and during certain individual years it had been 5 times greater. In spite of these discouraging findings, he continued to encourage the employment of tuberculous workers by the same concern, to which he was attached as industrial medical adviser. Some of these workers were still receiving treatment with drugs or pneumothorax refills.

The present report covers the 5-year period 1954–58, and deals with the same number as before, 119 tuberculous employees. Towards the end of this period about 10% of all the employees had a record of tuberculosis. Compared with the first period, the second period was hopeful. Indeed, for male workers there was little difference in the matter of absenteeism between the tuberculous and the non-tuberculous in this period, and during the last 3 years there was no such difference whatever. This improvement was most marked in the matter of early relapses which became much less frequent in the second period. Late relapses, on the other hand, occurred with the same frequency, the patients often being elderly. For female workers the figures continued to be comparatively discouraging. Natvig concludes that though his second period showed much better results than the first, there is a prospect of still better results thanks to closer supervision and the prolonged specific chemotherapy now in vogue. It should do much to reduce the incidence of relapses, not least the late relapses whose importance he emphasizes.

Claude Lillingston

See also p. 849, ARCH. MALAD. PROFESSIONNELLES, **[The Rehabilitation of Patients suffering from Pulmonary Tuberculosis.]**

HOPPER, J. M. H. **The Multiple-Puncture Method of BCG Vaccination in 13-Year-Old School Children.** *Med. Officer.* 1960, May 27, v. 103, No. 22, 311–15, 2 figs. [14 refs.]

In 1957 only 46·8% of the 630,004 children in England and Wales who were eligible for BCG vaccination under the scheme for school-leavers consented to take part; 237,502 were initially tuberculin-negative and only 233,256 were vaccinated (37%).

This very low acceptance rate was due to many reasons, among which were dislike of the injection, the occurrence of ulceration and scarring after intracutaneous vaccination and the resistance of teachers to the school routine being upset by the slow process of vaccination.

It was therefore decided to vaccinate by multiple puncture in 2 schools using the ordinary Heaf gun. In 1958 freeze-dried vaccine was reconstituted to a strength of 1·8 mgm./ml., and with this suspension each child was vaccinated by 3 triggerings of the Heaf gun (18 punctures) at 2 mm. depth. 248 children were thus vaccinated with a post-vaccinal conversion rate of 60%.

Because of the low conversion rate vaccine of a strength of 75 mgm./ml. was used in 1959 when 752 children were vaccinated. The number of triggering varied from 5 (30 punctures) to 7 (42 punctures) at 1 c 2 mm. penetration. The post-vaccinal conversion rat was 94·8% at 6 weeks or later. The deeper penetratio gave a higher conversion rate.

In 3% of those vaccinated by multiple-puncture ther was some breach of skin surface but in no case was ther ulceration such as may follow intracutaneous vaccinatior Pain was less marked than with injection. Scarring wa also less marked. The data presented do not provid positive evidence that multiple-puncture vaccination wi raise the acceptance rate as there are so many othe variable factors. The author however believes that th use of this method may help to increase the use of BCC vaccination in the 13-year-old school child and so con tribute to the lowering of the incidence of tuberculosis

H. G. Calwell

GESER, A. & AZUMA, Y. **Further Studies on th Heat-Stability of Freeze-Dried Glutamate BCC Vaccine: Effect of Storage at 30°–50°C on Aller genic Potency in Humans.** *Bull. World Healt Organization.* Geneva. 1960, v. 22, Nos. 1/2 171–6.

In this study the Japanese BCG vaccine, freeze-drie in the presence of 1–2% sodium glutamate, was com pared with the Danish liquid vaccine in 3 separat studies, 2 of them being in school children, aged 7– years, in Copenhagen and the third in school children aged 5–17 years, in Nigeria.

In the first study 52 children received Japanese drie glutamate vaccine that had been stored for 10 month in the refrigerator, 47 the same vaccine after it had bee stored for 8 months in the refrigerator and heated for months at 37°C., and 41 received the fresh Danish vac cine. Although the second study was with 153 children the number of variations of vaccine was 15 so the maxi mum number of children in any group was 14. Thi study included a Japanese dried sucrose vaccine and French dried glucose vaccine. The third group consiste of 368 children and these were divided into 5 groups, th largest containing 55 children. The children were teste with 5 TU of PPD 4–6 months after vaccination, an those of the third group were retested after a further 1 months. In all these studies the vaccination sites wer examined at the time of tuberculin testing.

The conclusions from the results are that:—(1) afte 17 months' storage under refrigeration the glutamat freeze-dried vaccine produces a tuberculin allergy a intense as that produced by the fresh liquid vaccine; (2 whereas storage at 30°C. for 1 month seriously impair the liquid vaccine it has little effect on the dried vac cines, but storage at 50°C. for the same period has deleterious effect; and (3) exposing the dried glutamat vaccine for 1 month to a diurnal variation of tempera ture ranging between 20° and 37° C., *i.e.*, tropical cond tions, has no deleterious effect.

[See also this *Bulletin*, 1957, v. 32, 84, 85.]

S. R. M. Bushby

VENEREAL DISEASES

FRIEDMAN, H. S. **Simplification of Certain Aspects in the Performance and Interpretation of Complement-Fixation Tests.** *Amer. J. Clin. Path.* 1960, Mar., v. 33, No. 3, 264–7.

The author describes modified rapid techniques for carrying out haemolysin and complement titrations in complement-fixation tests, together with a modified technique for reading the results. The technique requires only half as many pipettings as does the standard method. The 50% haemolytic and complementary units are determined by a spectrophotometric method and such a method is also used for reading the test itself.

The various dilutions used in the titrations are set out in tables and compared with those used in the standard method.

The techniques are described in very concentrated detail and those wishing to carry them out would require to study the original paper closely.

H. J. O'D. Burke Gaffney

BOKKENHEUSER, V. & RICHARDSON, N. J. **Reproducibility of Results obtained by the *Treponema pallidum* Immobilization Test in South Africa.** *South African J. Med. Sci.* 1959, Dec., v. 24, Nos. 3/4, 109–13, 1 fig. [17 refs.]

These authors carried out the TPI test in the usual way and generally added penicillinase to the sera before testing. For the test proper they employed 0·05 ml. serum, 0·3 ml. spirochaetal suspension (5–15 organisms per field) and 0·2 ml. complement equal to 36.4%. Reproducibility was estimated in 3 ways: (1) TPI 50–18 (dilution of a serum which immobilizes 50% of organisms after 18 hours) values of the suspension, with WHO reference sera, (2) duplicate investigations of a number of known sera, (3) results of tests carried out in Johannesburg and Copenhagen. Of 259 sera reactive at first, 234 (90·4%) were reactive on repeat; of 189 sera giving 90–100% immobilization, 186 (98·4%) remained reactive, therefore the error will only be 1·6%. Of 158 sera non-reactive at first, 1 was reactive and 6 weakly reactive on repeat; weakly reactive sera gave most trouble.

22 sera were sent to Copenhagen and agreement was found in all but 2; of these one was weakly reactive in Copenhagen and reactive in South Africa and the other the reverse in the 2 laboratories.

Thus the TPI appears to be satisfactorily reproducible [see also this *Bulletin*, 1956, v. 31, 145; 1957, v. 32, 950.]

T. E. Osmond

BOSSAK, H. N., DUNCAN, W. P., HARRIS, A. & FALCONE, Virginia H. **Evaluation of tpcf-50 Test and other TPCF Tests for Syphilis Diagnosis.** *Pub. Health Rep.* Wash. 1960, Feb., v. 75, No. 2, 130–34. [13 refs.]

The *treponema pallidum* complement-fixation test (TPCF1) employs a desoxycholate extract; this and a similar experimental one (TPCF2) were compared with the tpcf-50 which is claimed to be more specific and more economic of time and reagents [see PORTNOY, this *Bulletin*, 1959, v. 34, 1001]; the TPI test was carried out as well, mainly as a check. Sera were obtained from apparently healthy persons, persons with syphilis (early and late, treated and untreated), persons with diseases other than syphilis, including pinta and leprosy, and from suspected biologically false positive reactors (BFP). On 326 sera from healthy persons the reactivity percentage rates were TPCF1 13·5, TPCF2 21·47, tpcf-50 13·8 and TPI 2·76; on 497 sera from 8 different categories of syphilis, in primary and secondary syphilis tpcf-50 was the most reactive test, but in latent and late syphilis tpcf-50 was much less reactive than TPI although it agreed closely with TPCF1. In diseases other than syphilis, tpcf-50 agreed best with TPI. In the BFP tpcf-50 agreed most closely with TPI though it gave many more reactions. [It is of interest to note that of 109 sera considered BFP clinically, 38 (34·86%) were TPI reactive.]

T. E. Osmond

KIRÁLY, K. & PORGÁNYI, Maria. Antigenstruktur des *Treponema pallidum* (TP) und die Immunadhäsion (IA). [**Antigen Structure and the *Treponema pallidum* (TP) and Immune Adhesion (IA) Tests**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Feb., v. 119, No. 2, 183–95. [28 refs.]

A comparative investigation of the *Treponema pallidum* immobilization test (TPI) and the immune adhesion tests for syphilis was carried out with 264 sera. Among these there were 76 positive by older tests but negative by the TPI and classified as biological false positives (BFP). Of these 75 were also negative by the immune adhesion (IA) test.

The correspondence in these tests is best if care is taken to work with freshly prepared and undamaged treponemata. A variety of forms of digestion destroy the antigen responsible for this reaction, which seems to depend on absorption of complement which is produced by any treponemal antigens with appropriate antibodies.

J. W. McLeod

GARSON, W. & BARTON, G. D. **Problems in the Diagnosis and Treatment of Gonorrhea.** *Pub. Health Rep.* Wash. 1960, Feb., v. 75, No. 2, 119–23. [23 refs.]

These authors point out that the most effective clinical and pathological methods fail to detect the gonococcus in 25 to 50% of females and very wisely remark that the most sensitive indicator is the anterior urethra of a susceptible male; this latter emphasizes the desirability of epidemiological procedures. It has long been apparent that certain strains of gonococci are more resistant than others to penicillin and the findings of numerous

observers are set out in a table; therefore in the treatment of gonorrhoea the dosage of penicillin should be such that the serum level should be higher than that which any known strain can resist and should be maintained for at least 24, and preferably 48, hours. Further, if a long-acting preparation is employed it should kill any gonococci which have been temporarily protected within tissue cells and also prevent re-infection during the period when penicillin is active, which may be several weeks.

The dosage suggested is 1·8 mega units of PAM or 600,000 units of this plus 1·2 mega units of benzathine penicillin G. and when applied has resulted in a fall from 15% to 1·7% of treatment failures. Recent work on the gonococcus has shown that endotoxin is probably not a protein but a lipopolysaccharide phosphate; this suggests the possibility of finding a specific skin test, a specific antigen for serum testing and perhaps obtaining immunity against gonorrhoea. Fluorescent antibody techniques also hold out many possibilities [this *Bulletin*, 1960, v. 35, 179 and below.] *T. E. Osmond*

Deacon, W. E., Peacock, W. L., Jr., Freeman, Elizabeth M., Harris, A. & Bunch, W. L., Jr. **Fluorescent Antibody Tests for Detection of the Gonococcus in Women.** *Pub. Health Rep.* Wash. 1960, Feb., v. 75, No. 2, 125–9, 2 figs.

Specimens for examination were obtained from 100 women who were contacts of men suffering from gonorrhoea; these were taken in the ordinary way from vagina, cervix and urethra and were submitted to fluorescent antibody staining (FA) [this *Bulletin*, 1960, v. 35, 179], to the same but delayed (*i.e.* after preliminary culture), and to cultural procedures. The 3 methods—direct FA, delayed FA, and culture—in 50 patients proved positive in 26, 48 and 48% of vaginal, 8, 58 and 58% of cervical and 10, 44 and 40% of urethral specimens respectively; the success rates totalled 26, 58 and 58% respectively. In 100 women the direct FA was positive in 24 and the delayed in 58. Thus the delayed FA was at least equal to cultures and the combined FA's gave most positive results: FA is much easier and less time-consuming than culture. What is rather surprising is the large number of positive vaginal specimens.

Results are set out in 2 tables, and 2 figures are said to show typical gonococci stained by fluorescent antibody [but they will not convey much to the average reader who is not versed in these methods]. *T. E. Osmond*

Osterrieth, P. M. La réaction de déviation du com plément avec l'antigène de la lymphogranulomato vénérienne (maladie de Nicolas-Favre) chez l'ind gène de la région de Stanleyville (Congo belge [**Lymphogranuloma Venereum Complement-Fix tion Test in Africans of Stanleyville, Belgia Congo**] *Ann. Soc. Belge de Méd. Trop.* 1959, Oc 31, v. 39, No. 5, 663–74. [24 refs.]

In the region of Stanleyville in the Belgian Congo 1957 244,202 cases of venereal disease were reported which lymphogranuloma venereum (LV) represente 0·18%, though some people believe that it is much mo common than these figures suggest.

Sera from apparently healthy persons, syphilitic pe sons and children under 7 in hospital for various cond tions were subjected to a complement-fixation test (CF with commercial antigen, and some to the Frei test. 277 sera, 61 were positive with the CFT (22%); no chi gave a reaction; the percentage for the general adu population of Stanleyville was 18 but in those presume to have venereal disease it was 25 for Stanleyville and for persons from the interior; men gave more reactio than women, 37% as against 26% and the unmarrie more than the married, 41% against 31·9%.

In the Frei test on patients with venereal disease 6 o of 33 were positive (18·2%). Clinically out of 88 perso examined only 5 showed evidence of LV. It is pointe out that the LV CFT is only a group test and may rea in trachoma, urethritis and inclusion conjunctiviti however, psittacosis and these other conditions apparent do not occur in the Belgian Congo. The author co siders that the CFT is reasonably specific and that the are large numbers of latent cases of LV which would missed by clinical examination alone. *T. E. Osmond*

Wotherspoon, R. J. **A New Treatment for Vaginiti** *Practitioner.* 1960, May, v. 184, No. 1103, 626–8.

71 patients suffering from vaginitis were treated wi hexetidine (0·1%) marketed as "sterisil vaginal gel"; course of treatment lasted for 18–21 days; 30 patien had 1 course, 20 had 2 courses, and 21 had 3 course Of 32 with trichomoniasis, 17 were satisfactory, showed improvement, 3 were failures, 2 had reaction and 1 was unable to self-medicate; of 13 with candidias 6 were satisfactory, 4 improved, 1 had a reaction, and were failures; of 25 with non-specific vaginitis all we satisfactory but 1 with *Haemophilus vaginalis* faile Overall success was obtained in 48 (67·6%) and 6 we failures; 13 (18·2%) showed improvement. It is not e plained how the treatment was applied.

T. E. Osmond

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and Other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

ANN. NEW YORK ACAD. SCI. 1959, Sept. 1, v. 82, Art. 1, 1–190, numerous figs. [Numerous refs.] **Recent Contributions to Antibacterial Therapy** [RHOADS, P. S. (Conference Chairman)]. [Conference held May 21 and 22, 1959.]

The first half of this symposium deals with long-acting sulphonamides, sulphadimethoxine (Madribon), sulphamethoxypyridazine (Kynex) and sulphaphenazole (Orisul): all 3 are considered in the introductory pharmacological studies but in the clinical studies only sulphadimethoxine is studied in any detail. The advantages of these sulphonamides are that on a low dosage they have prolonged activity due to excellent absorption and very slow excretion: there is a low order of acetylation and the parent drug and its derivatives are readily soluble in the urine. The half life of sulphadimethoxine is 1 to 2 days and on once-daily dosage accumulation in the blood readily occurs. Toxic symptoms include headache, nausea, drowsiness, dizziness, rashes and psychoses—these are common to the older sulphonamides and they appear to occur in the long-acting sulphonamides mainly as a result of too high dosage: an initial dose for an adult of 1·0 gm. followed by a once-daily dose of 0·5 gm. produces satisfactory blood and urine levels of the drug; if the drug is given at intervals and in doses corresponding with the older sulphonamides then very high blood levels will occur and toxic symptoms result. On the other hand in one trial, 35 patients suffering from paraplegia and chronic cystitis were given a daily maintenance dose of 0·5 gm. with no toxicity and satisfactory control of urinary infection.

In 2 careful studies of the use of the drug in urological disorders, by M. SIERP and J. W. DRAPER (pp. 92–104) and W. S. KISER *et al*, (pp. 105–110) it is shown that the drug is useful in preventing and suppressing urinary infections, particularly infections with *Staphylococcus aureus*: even where the *in vitro* tests show that organisms are not sensitive, good *in vivo* results may be obtained, but as one author points out, many of the urinary infections treated nowadays have been exposed to a variety of antibiotics and other drugs so that it is not surprising if a new drug is far less than 100% effective.

Sulphadimethoxine has been used with success in children, especially for otitis and mastoiditis, tonsillitis and adenitis and respiratory infections. Under the age of 3 months, toxic blood levels may occur as the infant appears to have ineffective mechanism for dealing with the conjugation of glucuronides, in which form the drug is mainly excreted. If the drug is given to a pregnant woman at term, therapeutic blood levels may be expected in the cord blood within 5 hours. The drug has been used in the treatment of acne in daily dose of 0·5 gm. for 10 to 60 days with good results. It has also been used, rather uncritically, in a variety of respiratory and febrile conditions. It certainly appears to be a useful drug, properly used, and this symposium offers a good guide to such use.

The second part of the symposium deals with the evaluation of triclobisonium chloride (Triburon), a quaternary ammonium compound, in topical antibacterial therapy. Under experimental conditions, triclobisonium chloride was shown to be effective against *Streptococcus pyogenes, Staph. aureus* and, to a much less extent, against *Escherichia coli*: it appeared to be second to penicillin against streptococci, equalled neomycin against staphylococci but was much less effective than polymyxin B, neomycin and nitrofurazone against *E. coli*, though much more effective than bacitracin. In 2 groups, totalling 748 patients most of whom were suffering from pyodermata, the clinical results were regarded as good, especially when used with hydrocortisone: there was very little evidence of allergic reactions to the drug. The drug has been used in the treatment of acne vulgaris, in trichomonal and monilial vaginitis, and in rectal and perianal conditions: it has also been used for early and late burns and in a variety of plastic surgical procedures. The authors of the papers all seem satisfied that triclobisonium chloride is a useful antibacterial substance for topical application, having the virtues of antibiotic drugs without the disadvantages of sensitivity reaction.

A. B. Christie

J. AMER. MED. ASS. 1960, Apr. 30, v. 172, No. 18, 2044–5. **Blood Dyscrasias associated with Chloramphenicol (Chloromycetin) Therapy.** [Report to the Council on Drugs (KAUTZ, H. D., Secretary) by the Committee on Research (DE NOSAQUO, N., Secretary).]

The concluding paragraph of this short report is reproduced:—

"Although the subcommittee recognizes that chloramphenicol is a valuable antibiotic, it is also the opinion of the subcommittee that there is no longer a reasonable doubt that chloramphenicol may cause aplastic anemia. Periodic blood cell counts may be of some help; however, they cannot be relied on to detect signs of marrow toxicity sufficiently early so that chloramphenicol administration can be discontinued before an irreversible aplastic anemia develops. Therefore, judicious use of the drug must be the rule, and it should not be used prophylactically, in trivial infections, or in infections in which other, less dangerous antibiotics may be used effectively."

HOSPITAL AND OTHER CROSS INFECTIONS

DAVIES, D. M. **Staphylococcal Infection in Nurses.** *Lancet.* 1960, Mar. 19, 644–5.

There were 146 cases of staphylococcal infection among 725 nurses in the London Hospital in 1 year. This accounted for 16·4% of admissions to the nurses' sick

quarters and was responsible for an average loss of 8·5 working days. All lesions were of skin or soft tissues and 83% of them were on face, neck, axilla or upper limbs, 29% on the finger. The distribution of lesions suggested that direct contact was important in infection and the author wondered if the incidence could be lowered if the use of scrubbing brushes was discontinued. 98% of strains were penicillin-resistant, 33% were tetracycline-resistant, 4% chloramphenicol-resistant and one strain only resistant to erythromycin. *M. Patricia Jevons*

Dossena, G. & Sirtori, C. M. Ricerche sullo stafilococco piogene aureo in una clinica ostetrico-ginecologica. [**Researches on *Staphylococcus pyogenes aureus* in an Obstetrical Clinic**] *Ann. Sclavo.* Siena. 1960, Jan.–Feb., v. 2, No. 1, 39–68, 3 figs. [88 refs.]

The English summary appended to the paper is as follows:—

"The authors have searched for *Staphylococcus pyogenes aureus* in staff, in a group of mothers and new born children and in the air of some premises of an obstetrical clinic.

"In nursing staff many Staphylococcus carriers were found (29·50% in the course of a first investigation and 48% during a second examination carried out at a distance of time).

"The research in new-delivered mothers gave positive results in 45·5% (nasal swab), 29·2% (nipple swab) and 40% (milk).

"The umbilical swab taken in new born babies evidenced staphylococcus in 15·9% of the cases.

"The sensitiveness test to antibiotics of the strains isolated gave following results: penicillin 12·6%, erythromycin 99·1%, neomycin 81·6%, ambramycin 35%, terramycin 33·3%, aureomycin 32·5%, vulcamycin 100%, streptomycin 23·2%, polymyxin 0·44%, chloramphenicol 82·5%, bacitracin 94%, sulfathiazol 0. Of the 228 strains isolated, 128 (56·4%) demonstrated typable with the phages tested and 100 (43·6%) untypable. The most frequent phage types have been 83 VA_4, 47 C, 80, 80/52, 80/81/52, 29 and 6/47."

Hurst, Valerie. **Transmission of Hospital Staphylococci among Newborn Infants. II. Colonization of the Skin and Mucous Membranes of the Infants.** *Pediatrics.* Springfield, Ill. 1960, Feb., v. 25, No. 2, 204–14, 2 figs. [30 refs.]

The colonization of infants by *Staphylococcus aureus* was observed by daily swabbing of the nose, throat, rectum and 5 skin areas of newborn infants in 2 maternity units. In 1, all the infants became colonized in a least 1 site by the 3rd day of life; in the other 84% were still free of staphylococci on the 4th day. The reasons for this great difference were not fully discovered, but may have been related to differences in the types of staphylococci prevalent. Skin and rectum usually became colonized before the nose or throat; in 1 nursery the groin and axilla and in the other the umbilical stump were the areas earliest colonized. Different skin areas common had different phage types of staphylococcus.

[For Part I see this *Bulletin*, 1960, v. 35, 572.]

R. E. O. Williams

Berntsen, C. A. & McDermott, W. **Increased Transmissibility of Staphylococci to Patients receivin an Antimicrobial Drug.** *New England J. of Me* 1960, Mar. 31, v. 262, No. 13, 637–42. [12 refs.]

During 6 months in 1955, 294 men were admitted to ward in the Bellevue Hospital, New York, suffering fro various diseases. Any patients requiring antimicrobi chemotherapy were when possible given tetracyclin usually 1 gm. per day for about 11 days; a total of 12 had tetracycline, 130 had no antibiotic and 44 had oth drugs. Noses and throat cultures were taken on 5 da each week and examined for *Staph. aureus.*

Of 79 tetracycline patients who were non-carriers o admission, 36 (46%) acquired nasal staphylococci whil in the ward, compared with 15 (17%) of 86 untreate patients. Substitution of 1 staphylococcus by anothe occurred in 12 of 44 carriers in the untreated group, an in 24 of 41 carriers in the tetracycline group. Most c the treated patients who acquired staphylococci becam infected within the first week after admission. Tetra cycline treatment was associated with a decrease in th numbers of various non-pathogenic bacteria of the nos and throat. 12 of 38 untreated patients who acquire staphylococci, afresh or by substitution, gained antibiotic resistant strains, compared with 59 of 82 treated patient

R. E. O. Williams

COCCAL INFECTIONS

The Order in this section is:— *Staphylococcus Streptococcus, Neisseria, Others.*

Wallace, I. R. & Carson, N. A. J. **Staphylococca Septicaemia treated with Vancomycin in th presence of Chronic Renal Failure.** *Lancet* 1960, Mar. 5, 519–20, 1 fig.

Vancomycin is a powerful but dangerous anti-staphylo coccal agent. Like penicillin and streptomycin it i bactericidal in adequate dosage, and so differs from mos antibiotics. Its disadvantages are that it is poorly ab sorbed from the alimentary tract, and that it is highl irritant—it must therefore be given intravenously an in high dilution in order to prevent thrombophlebitis it is also apt to produce deafness unless the serum con centration is kept below 12 μgm. per ml., a level which is therapeutically effective but which can only be main tained by the aid of daily assays of the serum, especially in cases with diminished renal function.

A case illustrating this is described. A boy of 1 with bilateral hydronephrosis and a blood urea of 25 mgm./100 ml. had a drip-site infected with antibiotic resistant staphylococci and *Pseudomonas pyocyanea*

nd there was secondary purulent arthritis of the elbow-oint. Chloramphenicol and erythromycin given for 6 lays did not eradicate the staphylococci from the drip-ite or from the elbow-joint. A clear case was thus stablished for vancomycin, even though chronic renal ailure was present. The drug was administered into the nferior vena cava through a polyethylene catheter; the laily dose was 250 mgm. at first but was soon stabilized as a result of daily serum assays) at 75 mgm., and it vas injected in 5% glucose solution over a period of 4 iours. The catheter was kept patent by a continuous drip of 500 ml. 5% glucose daily. The staphylococci were eliminated both from the drip-site and the elbow-oint within 48 hours and recovery was rapid; the resi-dual *Ps. pyocyanea* infection of the drip-site was cleared by local treatment with neomycin.

Used in such desperate cases, and with due precautions, vancomycin can be a useful addition to the therapy of severe staphylococcal infection. *H. Stanley Banks*

Mendoza, F. & Neri, R. H. Epidemiologia de la fiebre reumática. [**Epidemiology of Rheumatic Fever**] *Salud Pública México.* 1960, Jan.–Mar., v. 2, No. 1, 83–104, 4 graphs. [89 refs.]

This is a review of some of the literature of the last 20 years dealing with rheumatic fever. Rheumatic fever is an important disease in some parts of Mexico, causing between one-third and one-quarter of all cardiopathies. The authors feel that urgent action is required in their country to deal with this disease, now, in part at least, preventable. *A. B. Christie*

Wannamaker, L. W. & Ayoub, Elia M. **Antibody Titers in Acute Rheumatic Fever.** *Circulation.* New York. 1960, Apr., v. 21, No. 4, 598–614, 2 figs. [74 refs.]

2 sets of laboratory tests are available for the study of rheumatic fever—(1) the "acute phase reactants," and (2) bacteriological and immunological studies. The first group includes the erythrocyte sedimentation rate and measures disease activity, but not only in rheumatic disease: the tests are useful for assessing clinical progress. The second group supply information about streptococcal infection and so help in the classification of the disease as rheumatic or non-rheumatic: they give no information about disease activity. This article is a study of the second group of tests. Antistreptolysin-O (ASO) determinations are the most useful, but some patients with rheumatic fever do not develop these antibodies and some normal people do. One or more secondary tests are therefore desirable and the authors recommend the anti-diphosphopyridine-nucleotidase (anti-DPNase or ASDA [antistreptococcal diphosphopyridine-nucleotidase activity]) test and the antideoxyribonuclease B (anti-DNAse B) tests. The first antibody may, *in vitro*, appear to be restricted to certain strains of haemolytic streptococci but, *in vivo*, it seems to be widely distributed. The second is widely distributed among group A streptococci and occurs regularly in patients following streptococcal infection. In patients with clinical evidence of rheumatic fever and high ASO titres there is of course no need for secondary tests. [This article is well worth reading in the original, especially by clinicians anxious to assess these tests.] *A. B. Christie*

New England J. of Med. 1960, May 5, v. 262, No. 18, 895–902. [10 refs.] **A Comparison of the Effect of Prednisone and Acetylsalicylic Acid on the Incidence of Residual Rheumatic Heart Disease. Combined Rheumatic Fever Study Group.**

This is a report by a Rheumatic Fever Study Group carried out in 8 hospitals in New York City, Baltimore, Boston and Cleveland. The object of the study was to compare the effect of corticosteroid and acetyl salicyclic acid therapy on the development of carditis in acute rheumatic fever. 57 children, aged 4 years to 12 years, were studied and the criteria for diagnosis of rheumatic fever and of carditis were strict. Prednisone was given to one group in a dosage of 60 mgm. daily for 3 weeks, then tapering off gradually for 9 weeks to a total dosage of 3 gm.; acetyl salicylic acid was given to the other group in a dosage of 50 mgm. per lb. body weight daily for 9 weeks, followed by 30 mgm. per lb. for 2 weeks and then by 15 mgm. per lb. for 1 week. Penicillin for the eradication of group A streptococci was given to both groups.

Prednisone was not found to be superior to acetyl salicylic acid in preventing residual heart disease. Both drugs appear to be able to suppress the inflammatory reaction caused by the disease, but in many patients, even if the acute symptoms are promptly and well controlled, cardiac damage is not prevented. None of the 28 patients given intensive and prolonged prednisone therapy showed serious side effects but the investigators felt that the results of the trial did not justify continuing with this mode of treatment.

[This is an important study the details of which cannot be easily summarized. No attempt was made in the investigation to study combined prednisone and acetyl salicyclic acid therapy.] *A. B. Christie*

Mou, T. W., Feldman, H. A. & Hartenstein, H. **Prevention of Recurrent Rheumatic Fever in Children and Adults with Oral and Repository Penicillin.** *Amer. J. Med. Sci.* 1960, Apr., v. 239, No. 4, 403–16, 2 figs. [23 refs.]

During a 3-year period, 139 rheumatic patients were given penicillin prophlyaxis in the form of either daily oral dosage of 200,000 units benzathine penicillin G or an intramuscular dosage of 900,000 units once a month. Both methods appeared to prevent or suppress Group A streptococcal infection and recurrence of rheumatic manifestations. Small increases of the anti-streptolysin O (ASO) titres occured in some patients in both groups and these were thought to represent subclinical streptococcal infections, the penicillin suppressing rather than completely preventing infection. The median ASO values in both groups showed a downward trend during the whole period. *A. B. Christie*

LATTIMER, Agnes, SIMON, A. J. & LEPPER, M. H. **Use of Sulfadimethoxine in the Prevention of Streptococcal Infections in Rheumatic Patients.** *Amer. J. Med. Sci.* 1960, May, v. 239, No. 5, 548–53, 1 fig.

The introduction of long-acting sulphonamides may have raised hopes of effective anti-streptococcal prophylaxis by once-weekly oral dosage. A previous trial of sulphamethoxypyridazine given once weekly showed that serum levels immediately before the weekly dose were too low for confidence in such a prophylactic schedule although an arbitrary level of 1 mgm. per 100 ml. was achieved in 73% of patients. In the present trial, sulphadimethoxine was given in a once-weekly dosage of 30 mgm. per kgm. body weight to 28 patients: a level of 1 mgm. per 100 ml. was achieved in 60%. This difference was not regarded as important but it seemed obvious that neither drug could be relied upon on a once-weekly dosage. *A. B. Christie*

BACTERIAL INFECTIONS

The Order in this section is:— *General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

PERETTI, E. Beobachtungen über Seuchenbewegung und über den Wert von Schutzimpfungen, insbesondere gegen Diphtherie und Scharlach. [**Changes in Epidemic Patterns of Diphtheria and Scarlet Fever in relation to Prophylactic Immunization**] *Gesundheitsfürsorge.* Stuttgart. 1960, v. 10, No. 2, 26–31, 2 figs.

In this paper the author gives some description of well-known observations on epidemic waves and the effect on these of active and passive immunization. There is recorded the experience of diphtheria in Grevenbroich in each year from 1933 to 1959. The area's population has increased from about 105,000 in 1933 to about 167,000 in 1958. Before 1939 when active diphtheria immunization of children was introduced the total number of recorded cases had risen from 57 in 1933 to 782 in 1938. In 1940 the number was 108 but in the war years rose to a maximum of 449 in 1944. A fairly steady decline followed and in 1959 only 3 cases were recorded. Tables give these figures by age incidence from which it is clear that since 1939 this incidence has increased proportionally in the over 14 age-groups.

Since 1943 active immunization against scarlet fever was combined with administration of diphtheria toxoid, and the reported incidence of scarlet fever has in general been reduced although this reduction has been by no means regular.

There is discussion of these experiences of the 2 epidemic diseases with due mention, in the case of scarlet fever particularly, of the influence on reported incidence of natural waves of infection, of the change in type of the disease and the fact that there is considerable conflict of opinion on the value of scarlet fever immunization.
M. E. Delafield

KEHR, M. J., TANNAHILL, R. W., ELIAS-JONES, T. F. WHITTAKER, L. **Observations on a Present-D Outbreak of Diphtheria.** *Pub. Health.* 196 May, v. 74, No. 8, 294–303. [11 refs.]

Certain clinical aspects of the 12 cases admitt during the 1958 outbreak of diphtheria in Essex [s below] are discussed. The patient who died, and patient admitted because of late palatal palsy had bo received antibiotic treatment for sore throat at home a no antitoxin was given in hospital. In the first ca diphtheria was not diagnosed until the appearance unmistakable cardiac symptoms on the 11th day disease, and he died from typical diphtheritic toxic my carditis on the 12th day. The second patient had t typical "bull neck" sign of malignant diphtheria, a was treated with large doses of antitoxin intravenous and intramuscularly on admission; she recovered aft passing through the complications of toxic myocardi with right bundle branch block, and of palatal paraly and right facial weakness. She had had tetracycline home for her sore throat, and throat swabs taken hospital were never positive. A third patient admitt with complete immobility of the palate 40 days after episode of "sore throat" was almost certainly the fi case of diphtheria in the outbreak.

In the other 9 cases an attempt was made to discov whether antibiotic treatment in the acute stage was inc cated in addition to antitoxin. It was concluded (and t reviewer from his own experience agrees) that, exce perhaps in laryngeal diphtheria, there is no solid a vantage in giving antibiotics in the acute stage of dip theria. A further point is the diagnostic problem pos in diphtheria masked by antibiotics. Throat swabs a then almost invariably negative, and a correct diagnos of diphtheria is largely dependent upon considerable e perience of the disease, with observation of such poin as pallor, listlessness, rapid pulse relative to the temper ture, and absence of marked anginal symptoms in t history. *H. Stanley Banks*

GROARKE, F. L., ADAMSON, M. I., ELIAS-JONES, T. & WHITTAKER, L. **An Outbreak of Diphtheri Epidemiological Aspects.** *Brit. Med. J.* 196 May 28, 1607–11.

This outbreak of *C. diphtheriae gravis* infection 1958, involving 12 cases and 14 carriers, had its origin an infants' school, and was of a type which may be e pected to recur in Britain unless a level of immunizatio against diphtheria, higher than that existing today can b regained and maintained. Of the 26 infected individua discovered in the course of massive swabbing of t schoolchildren and their contacts, 23 were pupils in t class in which the outbreak originated, or had a sib that class, or were closely associated with a known ca or carrier. Only 3 adult carriers were detected, and on 1 of the patients was under school age. Only 2 of t patients had been "completely" immunized with booster dose (given in 1950 and 1954 respectively); 9 the carriers had been actively immunized at some tim and 3 had been passively immunized with prophylact

rum. Of the 35 pupils in the affected class only 17 had een actively immunized, and of the 127 pupils in the hool only 60 could give evidence of immunization. The sease was clearly associated with the presence of over 0% unimmunized children in the community at risk. ut of approximately 3,000 swabs examined only 1 rrier was discovered who was not closely associated ith a known case or carrier.

The protective methods employed might well be copied subsequent similar incidents. They included: swabing of the pupils and staff of the school and of their milies and other close contacts; Schick-testing of all upils in the affected class, with passive-active immunizaon of those found to be Schick-positive and their subequent active immunization; isolation of all carriers ther in hospital or at home, and their treatment mainly ith erythromycin (which was successful except in 1 case here the tonsils and adenoids had to be enucleated efore a cure was obtained). The difficulty experienced distinguishing between some very mild cases and arriers is no new problem. *H. Stanley Banks*

ANTELEEVA, T. B. **Some Features of the Epidemiology of Whooping Cough.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 5, 59–67, 5 figs. [10 refs.] [Translated from Russian.]

The incidence of whooping cough in 1 district of Moscow during 1947–56 has been analysed in detail. During the 10 years the annual attack rate ranged from 6·5 to 59·5 per 10,000. The period covered 3 epidemics nd the largest outbreaks occurred with a peak incidence the winters of 1947–48 and 1954–55. The average onthly attack rates during the 10 years were at a minium, 2·9 per 10,000, in September and the maximum as 5 in December. The data were subdivided by groupng the patients by age and whether or not they attended hildren's organizations. The seasonal distribution of ttacks varied between the groups; among the children ho did not attend children's organizations there was a econdary peak in April-May but among children who ttended organizations this peak was postponed until ugust. There were other differences in the size of the ttack rates and position of the peak incidence between hildren who did or did not attend children's organizaons for the age-groups under 3 years and 3–7 years. hese differences the author states are due to differences environment and the consequent difference in character f contacts between the various groups.

W. J. Martin

HAW, E. B. & BRUYN, H. B. **Streptomycin in Therapy of *Hemophilus influenzae* Meningitis.** *J. Pediatrics.* St. Louis. 1960, Feb., v. 56, No. 2, 253–8. [11 refs.]

This is an excellent and timely review of the treatment f *Haemophilus influenzae* meningitis, based on an experince of 132 cases in infants and children in 2 hospitals ver a period of 10½ years. The results in each hospital, here the methods of treatment were identical, were pproximately equal. The combined mortality rate was 6·06%, and only 3 cases of subdural effusion were found (2·3%), although this complication was looked for in cases not responding rapidly to treatment. Late sequelae were demonstrated only in 3 cases in the combined series; there was, however, no follow-up except in cases reported abnormal after discharge from hospital. These are highly satisfactory results, which, indeed, rival those of any comparable series.

But the main point of this article is to draw attention to the value of retaining streptomycin as the key drug among the therapeutic agents used. Since chloramphenicol was discovered to be a rapidly effective drug in *H. influenzae* meningitis [PRATHER and SMITH, this *Bulletin*, 1951, v. 26, 854] there has been a tendency to use this drug exclusively and to drop streptomycin in the treatment of the condition. As chloramphenicol (given orally) may sometimes be rejected, or vomited, or poorly absorbed and exert only a bacteriostatic effect in unusual dosage, the authors consider that streptomycin, which in correct dosage is bactericidal, should always be given (intramuscularly, not intrathecally) preferably along with a sulphonamide, and that chloramphenicol should be *added* in all severe cases. The recommended dosage of streptomycin is 50 mgm. per kgm. per day for 5 days, and of sulphadiazine 150–200 mgm. per kgm. daily for 7–14 days. *H. Stanley Banks*

NEGRO, R. C., GENTILE, Irma & SCHIAFFINO, A. Tratamiento de la fiebre tifoidea en el niño con la asociación de córticoesteroides y cloranfenicol. [**Combined Steroid and Chloramphenicol Treatment of Typhoid Fever in Children**] *An. Facul. de Med. Montevideo.* 1959, v. 44, Nos. 5/6, 506–14, 3 figs. [28 refs.] English summary.

35 children whose ages ranged from 2 to 13 years suffering from typhoid (*Salm. typhi* isolated from the blood in 14, positive agglutination [no titres given] in 32) were treated with a combination of chloramphenicol and steroids. The grade of severity of the illnesses was, 2 slight, 21 moderate, 12 grave. The length of treatment which was as follows varied from case to case:— (1) chloramphenicol palmitate 50 mgm./kgm. body weight every 6 hours; only one-half or preferably one-third of this dose was given during the first 2–3 days, the dose was reduced by half after defervescence; (2) cortisone 100-200 mgm. daily according to the child's age in 14 cases; prednisolone 20-25-30 mgm. daily=approximately 1 mgm./kgm. in 21. The amounts were gradually reduced and if treatment had been prolonged corticotrophin was used finally instead. Vitamin C was also given.

In 12 who were receiving chloramphenicol on admission, fever fell within 2 days of the combined treatment being started; of 16 where combined treatment was started on admission defervescence occurred by the third day in 12; in 4 the temperature fell rather more slowly though the general state improved markedly within 24 hours. The enlarged spleen persisted for 2–3 weeks and ECG changes, which were noted in 16 patients, (prolongation of P-R, changes in T wave) for considerably longer. No complications occurred during treatment though some were present on admission.

In the text relapses are given as 4, but in all steroid treatment had either been suspended or was insufficient. The Widal when repeated showed raised titres still in 8 out of 14, in 20 faecal culture was negative. No deaths occurred and both drugs were well tolerated without side effects.

The authors consider the results extraordinary in 20 and excellent in 12. The severe toxic cases showed a fall in temperature within 3 days with great general improvement not met with on chloramphenicol treatment alone. They lay emphasis on the duration of the ECG changes even after apparent cure, but consider that this combined treatment is necessary in all cases of typhoid.

W. K. Dunscombe

FALK, W., NEEMAN, J. & ROSENFELD, J. [**The Treatment of Typhoid in Children with Corticosteroids and Chloramphenicol**] *Harefuah.* Jerusalem. 1960, May 15, v. 58, No. 10, [in Hebrew 309–12, 1 chart. (20 refs.) English summary 312].

In the Government Hospital, Haifa, during the period 1955–59, 38 children with typhoid fever (all in the "typhoid state") were treated with chloramphenicol (50 mgm. per kgm. body weight daily) and corticosteroids by mouth (20 mgm. per kgm. daily for those under 5 years; 40 mgm. per kgm. for those over 5). Usually the cortiscosteroids were given when chloramphenicol failed to produce rapid improvement, but for children in a serious condition they were given at once. Steroids were usually given for 3–7 days.

The response was dramatic. 6 of the 38 relapsed but this is about the same proportion as in other series treated without corticosteroids; there were no complications due to this treatment. The authors do not recommend the combined treatment for all cases of typhoid fever, but suggest its use in toxic cases or where chloramphenicol alone is not effective. *Charles Wilcocks*

HAENEL, H., KÖHLER, F., MERTSCH, H. & PARDEMANN, C. Über den Einfluss von Tetracyclinen auf die faekale Mikrobiozönose von TPE-Dauerausscheidern. [**The Influence of Tetracycline on the Bacterial Flora of Carriers of Typhoid, Paratyphoid and Enteritis (TPE) Bacteria**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 1, 41–61, 8 figs. [44 refs.]

This paper describes an immensely laborious study of the faecal flora in enteric carriers before, during and after treatment with antibiotics, specimens being examined at intervals over a long period by quantitative methods to assess the numbers of different groups or species of organisms. The findings are presented in large and complicated diagrams. The subjects were 8 patients in a mental hospital, 3 of whom were given tetracycline and 3 oxytetracycline, while 2 served as "controls". Two quite simple conclusions are reached. One is that the faecal flora of enteric carriers does not differ from that of normal subjects except in the presence of *Salmonella*. The second is that although tetracyclines cause this organism to disappear, it reappears when treatment is stopped. The effects of tetracycl treatment on the remainder of the intestinal flora w briefly as follows: no reduction in the total count; appearance of organisms of the *bifidus* but not of *acidophilus* group; no constant effect on *Escherichia* or "putrefactive" bacteria (undefined); an increase streptococci and *Proteus* and sometimes of fungi (p sumably yeast-like) and of staphylococci. When antibiotic was stopped the flora reverted to its origi distribution.

A minor but practical point is the finding that wh tetrathionate broth was inoculated from decimal dilutio of a faecal suspension, enteric organisms were most of isolated when the inoculum was a 10^{-5} or 10^{-6} dilut (34 and 32 positives respectively): from 10^{-2} only 8 w positive, and this is said to correspond to the size inoculum of solid faeces commonly used.

L. P. Garroc

BOKKENHEUSER, V. & RICHARDSON, N. J. **Salmonell and Shigellae in a Group of Rural South Afric Bantu School Children.** *J. Hygiene.* 1960, Ma v. 58, No. 1, 109–17. [36 refs.]

The Bantu children selected for this survey compri 124 pupils (67 girls and 57 boys) of a school in a Nat Reserve area in Western Transvaal. Their ages rang between 6 and 16 years. The children were examined times during a period of 1 year at fairly regular int vals. There was no serious clinical illness over the per and only a few cases of minor illness, yet of 75 child who attended all the examinations, 44.0% had at leas salmonella infection and 29·3% 1 shigella infecti Many of them were infected several times with differ organisms; 20 salmonella serotypes were isolated, apart from a small outbreak due to Salm. Mobeni types were isolated sporadically. Most of the shige strains isolated belonged to the Flexner group; type id tification was not done.

In the majority of cases the infections were s clinical and of short duration; there was no evide of long carriage of the infecting organism. The high incidence of the salmonella infections was in ea summer but the shigella infections were spread fai evenly over the year. *H. J. Benstec*

DARROW, D. C. & WELSH, J. S. **Recent Experience the Treatment of Diarrhea in Infants.** *J. Ped trics.* St. Louis. 1960, Feb., v. 56, No. 2, 204– [16 refs.]

14 years ago GOVAN and DARROW introduced th special electrolyte solution for intravenous use, conta ing potassium, which has since been widely adopted paediatric practice.

The study reported here was carried out on 307 fants, suffering from acute diarrhoea, admitted to Children's Mercy Hospital in Kansas City; it particularly directed towards the clinical status of hy natraemia, hypernatraemia and metabolic acidosis.

Hyponatraemia occurs whenever there is a dissocia

oss of sodium, the bodily water remaining little diminished, hypernatraemia when water alone is lost, in hich case both body Na and Cl will be high; metabolic cidosis is not directly related to the level of the reserves f either Na or Cl. The hydrogen ion concentration of ie body fluids in fact changes very little owing to the fficient buffer systems which operate, though replaceent of Na, K, Cl ions and water will ultimately be ssential for the restoration of the normal acid-base quilibrium. In states of acidosis the reduction of the icarbonate reserve is accompanied usually by the Na epletion or by a relative excess of Cl with a normal Na vel. K depletion however may accompany any diarrœal condition whether there be an actual depletion of a or not.

In 105 instances, concerning 102 infants, the concenation of plasma electrolytes was determined on admison. The balance was only mildly disturbed in 18, but as seriously altered in the remaining 87. Among the tter, the concentration of K was below 3 mEq. per tre in only 5 out of 84 examinations, and only abnorally high (above 6 mEq. per litre) in 17. In 104 estimaons of Na, only 15 were abnormally low (below 131 Eq. per litre), and only 11 abnormally high (above 150 Eq. per litre). The authors note that dangerous symptms, especially disturbances of cerebral function, rarely evelop in status of hypernatraemia, save at concentraons exceeding 150 mEq. per litre. They observe, owever, that serious acidosis and dehydration may occur ven in the presence of a normal Na concentration in ie plasma (*e.g.* 130–150 mEq. per litre). As regards the oncentration of Cl ions, levels below 95 mEq. per litre ere found only in 13 instances, and abnormally high oncentrations, exceeding 105 mEq. per litre in 53. In ie latter, the concentration of Cl ions might be disproortionately higher than that of the Na ions. Among 3 bicarbonate estimations only 20 entered the normal nge (more than 20 mEq. per litre), the remaining 68 l showing metabolic acidosis.

In treatment, Hartmann's lactate-Ringer solution is sed to replace electrolytes and water, being given in uantities of 60–80 ml. per kgm. body weight, together ith 20–40 ml. of [? 5%] glucose in water per kgm. ody weight. Maintenance fluids in addition to these eplacement solutions were infused in the following mounts per 100 calories per diem:— 120 ml. of (? 5%) ucose in water, 30 ml. of Hartmann's lactate-Ringer olution and 2mM (mille mols) of potassium chloride. arenteral fluids were usually required for the first 2 ays of treatment only, oral fluids in the form of glucose olution being administered towards the end of this eriod. Milk mixtures were then resumed at one-quarter one-half the normal concentration in amounts of 150 l. per kgm. daily. The Lytren milk preparation used s a routine in the Children's Mercy Hospital contined Na 50, K 20 and Cl 30 mEq. per litre.

An overall mortality of 4 out of the 307 infants admitted with diarrhoea compares favourably with other ublished reports. On the basis of this study the authors uggest that:—

(i) Diarrhoeal infants who show initially a high Cl oncentration, low bicarbonate and normal or nearly ormal Na concentration in fact are suffering from an absolute deficiency of bicarbonate, Na, K, and water. The last may require replacement in amounts of 100 ml. per kgm. body weight, while one-sixth molar sodium lactate may suffice to rectify the major electrolyte in balance.

(ii) Similarly affected infants who show initial hypernatraemia are in fact deficient in water and K. Acidosis may be present and may call for the administration of bicarbonate or lactate. Replacement is best affected by the administration of fluid in amounts of 100 ml. per kgm. body weight comprising 40–50 ml. of lactate-Ringer solution with 3–5mM of KCl, together with maintenance fluids.

[This exhaustive and detailed article is difficult to abstract and should be consulted in the original by those specially interested.] *J. H. Walters*

DOTTI, F. & CASETTA, R. Indagine epidemiologica sulla brucellosi in Provincia di Mantova. **[Epidemiologic Investigation on Brucellosis in the Province of Mantua]** *Igiene Moderna.* 1959, v. 52, Nos. 11/12, 705–12.

The English summary appended to the paper is as follows:—

"An investigation carried out during 30 months revealed 236 cases of human brucellosis. Basing on the epidemiologic data, it was concluded that the disease showed a sporadic appearance, except for some isolated epidemic episodes in the neighbourhood of infected stables. In general, only the rural population was affected, and, more precisely, people dealing with cattle.

"The need for more efficient and strict prophylactic measures is emphasized."

RAMACCIOTTI, F. E. La reacción de fijación en superficie en brucelosis. **[Surface-Fixation Test in Brucellosis]** *Rev. Facul. Ciencias Med.* Cordoba. 1959, Oct.–Dec., v. 17, No. 4, 289–96, 3 figs.

In the surface-fixation test, introduced by CASTAÑEDA, FAO/WHO Expert Committee on Brucellosis [this *Bulletin*, 1958, v. 33, 1131], a loopful of serum to be tested is placed on a strip of absorbent paper over a dried spot of *Brucella* antigen: loopfuls of known negative and positive sera are placed on adjoining spots and the strip is then dipped in saline. The saline rises into the strip and carries with it any negative sera: positive serum remains fixed by the antigen. 39 sera from patients in the acute phase of brucellosis all gave a positive surface-fixation test and 38 a positive agglutination test, one showing the zonal phenomena in the first 2 tubes. Of 93 sera from patients in the acute and chronic phases, 78 gave positive agglutination and complement-fixation tests, and 76 positive surface-fixation tests. The author feels the test should be more widely used, as it can be carried out without the help of a specialized laboratory and it eliminates the zonal phenomena, the blocking tests and agglutinations due to vaccine therapy.

A. B. Christie

RIGBY, E. P. **The Increasing Importance of Tetanus in Kenya.** *East African Med. J.* 1960, Jan., v. 37, No. 1, 1–8.

Only one of the 33 countries in Africa had a higher mortality from tetanus than Kenya in 1955. Tetanus with 258 deaths was the fifth most important cause of death in Government hospitals in 1957. The admissions for tetanus have increased 21 times since 1933, while the total admissions have only increased 5 times. The average case mortality during the 9 years 1948–56 was 39%. The author has considered whether the rise in the number of admissions could be due to one or more of the following factors (a) increase in population, (b) increase in the popularity of the hospital services, (c) expansion of hospital services, (d) introduction of new and more effective treatment, (e) increase in the incidence of the disease. The evidence points to a real increase in disease. There is a geographical distribution of the incidence and the agricultural districts have a higher incidence than the pastoral. The author thinks that this is due, in part, to the increasing use of animal manure in recent years. He concludes that it is certain that the incidence will continue to rise, and protective inoculation should be carried out. Triple vaccine is available through child-welfare centres and plans are being made for the inclusion of tetanus toxoid with TAB vaccine. *W. J. Martin*

TOOGOOD, J. H. **Allergic Reactions to Antitetanus Serum.** *Canadian Med. Ass. J.* 1960, Apr. 30, v. 82, No. 18, 907–12. [14 refs.]

The author discusses the incidence in Canada of the disease he calls anti-tetanus serum allergy. He estimates that 7,900 severe cases occur annually and that approximately 31,500 working days are lost owing to the disease. Mortality is difficult to assess as deaths may not be certified as due to ATS allergy. He gives details of the deaths of 2 patients: in 1, death followed 10 minutes after an intradermal test in an asthmatic patient, in the other, death occurred from haemorrhagic encephalitis 13 days after the administration of 1,500 units ATS which had been given after a negative scratch test. The author states that the dilutions usually recommended for test doses are dangerous and that dilution of at least 1 in 1,000,000 is necessary. The whole practice of ATS prophylaxis is unsound and should be replaced by active immunization. *A. B. Christie*

FULFORD, G. E. **The Prevention of Tetanus.** *Lancet.* 1960, May 21, 1121–3. [15 refs.]

Anti-tetanus serum (ATS) is an unsatisfactory prophylactic for several reasons. Tetanus may follow trivial injury for which anti-tetanus serum is not given. ATS may produce serum reactions, many mild, many severe, the rare one fatal. A patient who has had ATS may develop the ability to excrete the antibody very rapidly so that a dose given for a second injury may be ineffective. The only satisfactory prophylactic is active immunization. If a patient is given ATS after an injury, he should also be offered a course of 3 injections of teta toxoid. If a patient has previously had ATS he sho be given toxoid rather than ATS. All patients wit breach of the epithelium should be given a course toxoid. All infants should have tetanus toxoid inclu in their immunization programme. In this way a h level of active immunization could be built up in community and the prophylactic use of ATS wo cease. *A. B. Christi*

RÉTHY, L., RAUSS, K., KÉTYI, I. & MARÓCZI, J. **Stud on the Immune Effect of *Shigella* and Tetar Antigens combined with "Booster" Antige** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 93–101. [12 refs.]

This paper is concerned with the immune response combined prophylactics in children who already poss some basal immunity to one of the antigens in the com nation as a result of previous immunization. The auth prepared a series of simple and combined prophylact against typhoid, tetanus, diphtheria, pertussis and shige organisms. Adsorbents of different strengths and co position were used. Children, aged 12–13 years, w different inoculation histories were selected for the tri Some of these children had not been previously imn nized, others had received typhoid-tetanus antigens a yet others had received diphtheria-tetanus-pertussis p phylactics. There were also differences in dosages a intervals. Re-vaccination with the combined antigen p parations described, failed to show that the immune eff of the booster antigen in the preparation used for re-inoculation trials was significantly different in the p inoculated and in the previously un-inoculated childr For instance, in children previously inoculated w typhoid vaccine, re-inoculation with typhoid-tetanus p phylactic produced an antityphoid response which w not statistically different from that seen in children w had not previously been immunized against typho The authors claim that the absence of any interferer effect of combined prophylactics, indicated by otl workers in this field [this *Bulletin*, 1955, v. 30, 826; 19 v. 31, 993; 1957, v. 32, 226], could well be explained the particular composition of the prophylactics they e ployed. It is difficult to argue this point.

H. J. Benstea

TURNER, L. H., ELISBERG, B. L., SMITH, C. E. G. BROOM, J. C. **Acute Febrile Illnesses in Malay Leptospirosis.** *Med. J. Malaya.* 1959, Dec., v. No. 2, 83–98. [15 refs.]

Interest in leptospirosis in Malaya, dormant sin Fletcher's original studies in 1928, was stimulated by t appearance of the disease among Army personnel oper ing against bandits throughout the country from 19 Studies by military medical authorities have establish that:— (i) leptospirosis is a common cause of acu fevers in some parts of Mayala, (ii) the disease in th country is seldom severe, (iii) diagnosis by simplifi laboratory techniques can be carried out in Malaya, a

v) the animal reservoirs are not yet fully defined but re under active investigation.

It is probable that many anicteric cases occurring mong the civil population escape recognition. Thus ough official returns have recorded only 153 cases with 0 deaths during a period of 5 years and 9 months over ne whole of Malaya, in a special study into the causes f acute pyrexia among 238 Asian patients, leptospirosis as confirmed in 13% [McCrumb *et al.*, this *Bulletin*, 957, v. 32, 954]. These authors also reported that lepto- pirosis was the commonest cause of acute pyrexia ccurring among troops operating in Perak, Selangor, ahang and Negri Sembilan, the incidence being 35% f all such illnesses.

The test used for screening numbers of sera, here des- ribed by the authors, is the sensitized erythrocyte lysis SEL) test, sometimes called the haemolytic (HL) reaction. : is genus-specific only. The antigen is prepared y chemical extraction of cultures of *L. biflexa.*

With the SEL reaction a 16-fold rise in the titre of aemolysing antibody in the second of paired sera taken uring the acute illness is indicative of a recent lepto- piral infection, as is an initial titre of 160 or over. ince SEL antibodies develop early in the disease, a iagnostic titre will usually have been attained by the me the patient presents himself, and little further rise ill occur during the next week. In non-febrile subjects titre of 80 is suggestive of past infection.

Employing this reaction, the authors have carried out ntibody surveys in various population groups, with the llowing incidence of positive reactions:— Kuala umpur residents, 9%; out-station residents 10%; ante- atal patients, in Kuala Lumpur, 18%. Earlier surveys ave shown the following incidences:— village Malays 7%; urban Chinese 20%; Sakai (aboriginals) 50%; rban meat handlers 26%; population of Bukit Meriam, outh Kedah 29%.

The clinical manifestations of leptospirosis are so aried and inconstant for any one serotype that it would e wise to abandon names of such a narrow specificity, as Weil's disease (*L. icterohaemorrhagiae*) and canicola ever (*L. canicola*), since their clinical differentiation is arely possible.

Leptospiral diseases in Malaya as a whole show the llowing characteristics:— abrupt onset, headache and neningeal irritation in one-third of patients, conjunctival njection, muscle tenderness, anorexia, nausea and vomit- ng, cough, haemorrhagic phenomena in one-quarter, sually as haemoptysis haematemesis, melaena, epistaxis, ub-conjunctival haemorrhages and petechiae. Clinical aundice is uncommon, and palpable enlargement of the iver and spleen is also uncommon.

Complications are rare: such as occur in Malaya have een thrombophlebitis, pyelitis and anaemia; recovery sually ensues spontaneously in 3–14 days, the usual uration being 8 days; the mortality is low, of the order f 3%. The following laboratory findings should be oted:— the leucocyte count is usually normal, the pro- ortion of neutrophil polymorphs is usually increased; rinary abnormalities may not develop in mild cases and ay not develop for several days in more severe examples f the disease; the level of the blood urea is of consider- ble prognostic significance; liver function tests may give normal results and in any case carry no diagnostic signifi- cance; cerebro-spinal fluid changes, comprising a poly- morphonuclear pleocytosis and an increase of protein, may occur even in the absence of signs of meningeal irritation.

Treatment requires the careful maintenance of fluid and electrolyte balance, since renal failure is the com- monest cause of death. Penicillin in large doses—3·6–5·0 mega units per day—should be injected as soon as the disease is suspected, since this prompt administration appears beneficial whereas delay in an effort to establish the diagnosis will nullify the chances of success. A Jarisch-Herxheimer type of reaction may occur in 80% of patients treated with penicillin [*ibid.*, 1958, v. 33, 344] and is regarded as a good prognostic and indeed a valuable diagnostic sign. Oxytetracycline, given orally in a loading dose of 1·5 gm. followed by 0·5 gm. every 6 hours is probably equally effective, but chlortetracycline is less well tolerated, and chloramphenicol appears in- effectual. Pethidine is a useful analgesic but severe head- ache may require lumbar puncture for its relief.

Important reservoir hosts include certain rats, especi- ally *R. norvegicus, R. argentiventer* (the ricefield rat) and the ground-living forest rats, the pig, the goat, the dog, the domestic cat, the civet cat, and (surprisingly) snakes.

Control of the disease is difficult to achieve, for reser- voir hosts cannot be eliminated, the infected environment cannot be sterilized and no vaccine efficient against the wide range of serotypes existing in Malaya has yet been produced. [This is a valuable, authoritative review, which merits study in the original.] *J. H. Walters*

Brown, R. Z. & Gorman, G. W. **The Occurrence of Leptospiral Infections in Feral Rodents in South- western Georgia.** *Amer. J. Pub. Health.* 1960, May, v. 50, No. 5, 682–8, 2 figs. [12 refs.]

" Between October, 1953, and July, 1955, 2,673 rodents representing 10 species were collected from 28 habitats in southwestern Georgia, and 933 were tested for lepto- spires by culturing kidney tissue. L. ballum was the only serotype isolated. Positive cultures were obtained from 22% of the house mice, 0·8% of the oldfield mice, and 1·9% of the cotton rats. Positive specimens, regardless of species, were collected almost exclusively from habitats supporting large house mouse populations. Infection rates in house mice ranged between 30 and 35% in most habitats ecologically suited to sizable house mouse popu- lations."

Warfolomejewa, A. A. & Lawrowa, M. J. Lepto- spirosen herde und ihre Klassifikation. [**On Cen- tres of Leptospirosis and their Classification**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 2, 230–38. [17 refs.]

Kathe, J. Leptospirose als Berufskrankheit. [**Lepto- spirosis as an Occupational Disease**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 3, 316–28, 8 figs. [Numerous refs.]

This paper has as introduction some account of the history in Germany of industrial diseases entitling to

compensation. In 1943 the zoonoses transmissible to man were added to the list of these diseases. There follows a statement of the conditions which must be fulfilled before doctors should accept any case of infection as one of occupational leptospirosis.

Weil's disease is the most frequent of the leptospiroses in man and some statistical information concerning the prevalence of the disease in the German Democratic Republic is given. In the period 1945–58 a total of 240 cases in man with 17 deaths was notified but the actual number was probably greater. Estimates of the rat population indicate that the density of this is 1 rat per person. Examination of 1,200 Berlin rats showed that in the aggregate 10% of these were infected with leptospires, but in 1 locality where the food supply was good the percentage was 40%.

Attention was directed to leptospirosis in factories where food is handled and a large number of serological examinations were carried out, the results of which are tabulated. In a sample of 105 of the general population only 1 gave a positive to *Leptospira icterohaemorrhagiae*, but among 1,951 persons in certain occupations 4·8% of positives were found. High figures were found in a fish factory (8%), a slaughterhouse (26%), in sewer workers (13·2%), workers at a zoo (15·2%) and at a research institute (5 out of 31 persons or 16%).

Some description is also given of *Leptospira canicola* infection which though much less common than Weil's disease may occur as an occupational disease among persons who come into contact with dogs.

Leptospira grippotyphosa infections also occur sporadically or in small groups in certain parts of the Republic and are in some instances to be regarded as cases of an occupational disease. *M. E. Delafield*

GARDNER, D. L., PINES, A. & STEWART, Sheila M. **Fulminating and Fatal Pneumonia and Septicaemia due to** *Achromobacter anitratus*. *Brit. Med. J.* 1960, Apr. 9, 1108–9.

The authors describe 1 case of pneumonia and septicaemia considered to be due to *Achromobacter anitratus*, an organism originally described by SCHAUB and HAUBER [this *Bulletin*, 1949, v. 24, 161]. The patient, a man aged 50 years who suffered from chronic bronchitis and congenital cystic disease of the kidney, died within 24 hours after a rigor which was the first symptom of illness. Post-mortem examination showed a confluent bronchopneumonia involving most of one lung, severe congestion of the other lung, and small haemorrhages in the cortex of each adrenal. The evidence suggesting that *A. anitratus* was the causative organism was the isolation of this species as the predominant organism cultured from a specimen of sputum obtained before death, and the presence of Gram-negative diplococci in smears of bronchial pus at necropsy, inside polymorphs in histological sections of lung and spleen, and lying between cortical cells in sections of adrenal. The strain of *A. anitratus* isolated from this patient differed from Schaub and Haubner's original strain in forming acid in xylose and in failing to show the methyl red reaction. [The authors state that there has been no convincing evidence previously published of the pathogenicity of this organism for man. They do not mention the report by SIMPSON and CROSSLEY (*ibid.*, 1955, v. 30, 168) of 96 isolations of the organism including 3 from cases of meningitis in a newborn and 1 from a case of pneumonia and septicaemia. Neither do they discuss the probability that the same organism has been reported as the cause of pneumonia, septicaemia and meningitis, under the name *Mima* (see OLAFSSON *et al.*, *ibid.*, 1958, v. 33, 705; FAY and HOOD, *ibid.*, 1950, v. 25, 755).] *I. B. R. Duncan*

VIRUS INFECTIONS

The order in this section is:—*General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.*

JONCAS, J. & PAVILANIS, V. **Diarrhoea and Vomiting in Infancy and Childhood: Viral Studies.** *Canadian Med. Ass. J.* 1960, May 28, v. 82, 1122, 1108–13. [12 refs.]

This paper reports the results of virus investigations in sporadic and epidemic cases of childhood diarrhoea and vomiting seen in hospital practice in Montreal from July 1958 to May 1959. Patients in whom bacterial infections or other non-viral causes of diarrhoea could be eliminated were examined by rectal swabs; these were inoculated into HeLa and primary monkey kidney tissue cultures, and 2–4 passages were made from each specimen.

From 74 subjects the total virus isolation rate was 19%, compared with 8% in a group of 62 hospital controls with non-infective chronic illnesses. More than 50% of the viruses obtained from each group were adenoviruses; the specific type recovered varied in epidemic fashion throughout the year. Total numbers are too small to determine whether any given type was truly more common than in controls. Paired sera from 28 patients showed significant rises in complement-fixing antibody to adenovirus in 7, from 5 of whom no virus isolation was made from rectal swabs. The clinical picture in the cases with evidence of adenovirus infection appeared to vary according to age, the infants showing a similar diarrhoea and vomiting and the older children additional respiratory symptoms.

From the rest of the infective groups no definite pattern emerged. [Since paired sera were not tested from each child and no throat swabs were taken, the total incidence of adenovirus infections could well be higher than that reported.] Poliovirus type I was found in 1 child and poliovirus type III in 1 other. 1 Coxsackie infection (type B_5) was found in the diarrhoea children, and 1 in the controls; there were 2 ECHO infections in the diarrhoea children and 1 in a control. *Derek Hobson*

NANIKIAN, A. M. & BAROIAN, O. V. **Use of the Chick Embryo Aldolase Reaction in the Diagnosis of Disease of Virus Origin. Preliminary Communication.** *Problems of Virology.* London. 1959, v. 4, No. 3, 73–9, 3 figs. [Translated from Russian.]

" (1) The aldolase activity of the allantoic fluid of chick mbryos is appreciably changed by a number of infec- ous agents of virus origin.

" (2) A regular rise in aldolase activity was observed the allantoic fluid after infection of chick embryos ith types A, A-prime and B influenza virus. The specifi- ty of this phenomenon was demonstrated by the fact at it was neutralized by specific immune serum.

" (3) When measles virus was used for infection a rise aldolase activity was noted in a considerable propor- on of chick embryos. There was a correlation between is reaction and the results of the complement-fixation st with specific antiserum.

" (4) The neurotropic viruses of Japanese B and tick- orne encephalitis and West Nile fever produced no ange in the aldolase activity of the chick embryos.

" (5) Agreement was observed between the rise in ldolase activity in chick embryos injected with the serum f patients with infective hepatitis and the clinical and aboratory findings for the donors of the serum. It was ot possible to inhibit this phenomenon in neutralization sts with convalescent sera."

[See this *Bulletin*, 1954, v. 29, 1000.]

HRENGUT, W., SCHEPPE, K. J. & JOAS, E. Intralumbale Hydrocortisonanwendung bei postvakzinaler Enzephalitis. **[The Intralumbar Administration of Hydrocortisone in Postvaccinal Encephalitis]** *Deut. med. Woch.* 1959, Nov. 6, v. 84, No. 45, 2005–6.

This paper contains an interesting clinical account of case of post-vaccinal encephalitis in which the patient ade full and rapid recovery after the administration y lumbar puncture of hydrocortisone, a method of treat- ent which has been recorded as of value in other forms f encephalitis [this *Bulletin*, 1957, v. 32, 428.]

The patient, a healthy normally developed infant was accinated against smallpox at the age of about 7 onths. On the 13th day after vaccination the child ecame irritable and collapsed suddenly with difficulty breathing and some cyanosis. A doctor gave treat- ent and sent the infant to hospital where the patient, ow unconscious, was considered to be moribund with xtreme respiratory difficulty, cyanosis, tachycardia, ever of 39·2°C., nystagmus but no meningismus. The eatment which is fully described was energetic but 5 ours after admission the child's condition appeared to be opeless. Hydrocortisone (25 mgm. in crystalline suspen- on) was then administered by lumbar puncture. After hours there was marked improvement in the general ondition. The infant had a quiet night and in the orning was as though transformed. It had red cheeks, good appetite and took interest in its surroundings. fter 8 days there was complete recovery.

It is believed that this method of administration will give valuable results but that it should be used early before cerebral oedema has caused serious damage.

M. E. Delafield

LEVIN, S. **Cerebellar Ataxia following Chickenpox.** *Lancet.* 1960, June 4, 1222–3. [17 refs.]

A boy aged 7 years, on the 8th day of a hitherto mild attack of chickenpox began to develop signs of central nervous involvement—headache, vomiting, pyrexia, slurred laboured speech, some clouding of consciousness and mild meningism. Cerebrospinal fluid was not examined. Later, the boy became grossly ataxic, but after about a month he appeared to have recovered completely.

J. Pickford Marsden

GIBEL, H., KRAMER, B. & NAJI, A. F. **Encephalitis complicating Chickenpox. Report of a Case with Death Two and a Half Years Later, and Review of the Literature.** *J. Dis. Children.* Chicago. 1960, May, v. 99, No. 5, 669–79, 3 figs. [41 refs.]

This patient was studied intensively over a period of 2½ years. He was first seen at the age of 3 years when he began a series of episodes of coma associated with acidosis and many confusing variations of blood chemistry alternating with periods of normality. All this followed an attack of chickenpox; the first symptoms—extreme lethargy—being noticed almost 1 week after the onset of this illness. During the 2½ years the child was admitted to hospital on 5 occasions; the original text must be consulted for details of the very many investigations carried out. After death the basal ganglia and the internal capsule on both sides were found to be the seat of focal haemorrhages. Examination of sections from lesions in the brain involving the caudate, putamen, globus pallidus and thalamus, showed loss of internuclear demarcation, marked distortion and fragmentation with extensive decrease in neurons. Areas of recent focal haemorrhages were present with zones of perivascular infiltration by lymphocytes, monocytes, plasma cells and occasional polymorphonuclear cells. These changes are illustrated in the 3 plates. The authors review the literature of chickenpox encephalitis.

[This was certainly a very unusual case by virtue of its chronicity, relapses and unexplained biochemical changes.] *J. Pickford Marsden*

TAYLOR-ROBINSON, D. **Herpes Zoster occurring in a Patient with Chicken-Pox.** [Memoranda.] *Brit. Med. J.* 1960, June 4, 1713, 1 fig.

LIPPI, M. & CORSO, P. Contributo siero immunologico alla conoscenza delle principali virosi. Ricerca nei soggetti sani degli anticorpi devianti il complemento verso il virus erpetico. **[Complement Fixing Antibodies against Herpes Virus in Healthy Persons in Rome]** *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, May, v. 41, No. 5, 227–60, 1 fig. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The serum-antibodies fixing the complement to a herpes antigen have been studied in a sample of the healthy population of Rome, including 126 individuals.

"In 19% of the examined sera there was evidence of anti-herpes anti-bodies at a titre higher than 1:4."

LENNETTE, E. H., CAPLAN, G. E. & MAGOFFIN, R. L. **Mumps Virus Infection simulating Paralytic Poliomyelitis. A Report of 11 Cases.** *Pediatrics.* Springfield, Ill. 1960, May, v. 25, No. 5, Pt. 1, 788–97. [19 refs.]

Case reports are given of 11 children, aged 2–8 years, all of whom appeared to be suffering from mumps meningo-encephalitis confirmed serologically. Each child had some muscle weakness during the acute stage and 4 had slight residual weakness 2–5 months later. Poliomyelitis virus was absent from the stools and there was no serological evidence of infection with poliomyelitis. [This is an important and interesting article in view of the occurrence of poliomyelitis-like illnesses in immunized patients.] *A. B. Christie*

ZHDANOV, V. M. & STAKHANOVA, V. M. **A Study of Human Sera for Antihaemagglutinins to Influenza-Like Animal Viruses.** *Acta Virologica.* Prague. 1960, May, v. 4, No. 3, 187–8.

"1. Sera from persons of different age groups did not contain antihaemagglutinins to duck and equine influenza viruses.

"2. Antihaemagglutinins against swine influenza virus were present in sera from persons aged over 40 years."

SJÖBERG, B. **Experiments on Prophylaxis and Suppression of Epidemic Influenza with N^1,N^1-Anhydrobis-(β-Hydroxyethyl)biguanide-Hydrochloride (ABOB). A Double Blind Study.** *Antibiotic Med.* New York. 1960, Feb., v. 7, No. 2, 97–102.

Although the recently recorded effect of ABOB on experimental influenza in mice [this *Bulletin*, 1960, v. 35, 820] is acknowledged to be "marginal", the drug has been submitted to clinical trial. It was first given to cases of "upper respiratory infection with probable virus etiology" and a few of mumps, with encouraging results; then tried in smallpox in Korea with apparently inconclusive or negative results. The 2 principal trials recorded were in influenza: these were double-blind trials, half the patients receiving inert tablets and half 100 mgm. ABOB twice daily for 6 days or longer. The patients were soldiers, the author being on the Swedish Army Medical Staff. The first trial was in an influenza A epidemic: both subjectively (in terms of time to recovery in the patient's own estimation) and objectively (temperature fall) there was a highly significant difference in favour of the treated group. A second trial was in an epidemic due to Asian-type virus. The tablets used in this also contained 0·1 mgm. each of methatropine nitrate and methscopolamine nitrate and the dose of ABOB was increased to 200 mgm. 3 times a day. similar therapeutic effect was obtained (fewer de given) and some evidence of prophylactic efficiency: 54 men at the height of the epidemic treated with AB for an unstated period, 11 developed influenza: of controls, 29 did so. *L. P. Garro*

GUSTYREV, V. F. **The Duration of Postvaccinal I munity in Individuals vaccinated with L Influenza Vaccine.** *Problems of Virology.* Lond 1959, v. 4, No. 2, 27–32. [28 refs.] [Transla from Russian.]

The persistence of immunity following vaccination v live influenza virus was investigated by compar haemagglutination-inhibiting antibody titres in vaccinated and 222 control volunteers. Two batches vaccine, both containing influenza A, A1 and B stra were used after preliminary tests for ability of the viru to multiply in human subjects. Antibody respon mostly to single virus types were found in 80·7% vaccinated subjects and in 10·8% of controls. The a body titres reached a maximum at 1½ to 3 months a vaccination and fell off first gradually and then stee during the next 5 months but was still above the p vaccination levels at the end of this time.

H. G. Pereir

STILLE, W. T. **Protection and Infection Rates Influenza and Adenovirus Vaccine Evaluatio** *Amer. J. Hyg.* 1960, Mar., v. 71, No. 2, 129– 1 fig.

Many studies have been published in which the eff tiveness of influenza and adenovirus vaccines was e mated by comparing the incidence of illness in grou injected with vaccine with the incidence in others ceiving a placebo. Laboratory tests have often be made to determine the cause of the illnesses in su groups. Data from 23 studies of this sort (14 unpublish were analysed in this paper. For each study the auth lists (i) the apparent reduction of clinically evident ness, and (ii) the proportion of cases of illness in control group (unvaccinated) in which laboratory te showed that the patient was infected with the type virus used in the vaccine. The 2 quantities seem to directly proportional to one another when 2 of studies are excluded (because inert or inappropri vaccine was used). The author concludes that the vacci almost completely prevented illness due to the vi used, and that the virus infections detected by laborat tests in vaccinated subjects were not causing disease. suggests a new statistic, the Intrinsic Vaccine Effic (IVE)

$$\text{IVE} = \frac{\text{clinical relative reduction (\%)}}{\text{control patients infected (\%)}} \quad 100$$

and indicates under what conditions it may be valid.

It seems that this method of analysis might avoid difficulty of interpreting serological tests in vaccina subjects whose antibody levels are high while using

esults of laboratory tests to reduce the "obscuring" of vaccine protection when there is much disease of unknown aetiology; however it is obvious from the data presented that fallacies may arise and the method will have to be used with caution. *D. A. J. Tyrrell*

LENNETTE, E. H., FLINTJER, J. D., CULVER, J. O., FOX, Virginia L. & STEVENS, Thirza E. **Adenovirus Vaccine: Evaluation of Antibody Response and Protective Efficacy and Comparison with an Earlier Preparation.** *Amer. J. Hyg.* 1960, Mar., v. 71, No. 2, 193–203, 1 fig. [10 refs.]

This paper reports a careful study of the increase in neutralizing and complement-fixing antibodies in 49 men receiving adenovirus vaccine containing types 3, 4 and 7 of virus "fine-filtered" and inactivated with a 1/400 dilution of formalin. The effect of this vaccine on the numbers requiring admission to hospital because of respiratory disease was studied by inoculating and observing up to 786 military trainees. Up to 1,950 received a placebo control preparation. The men were observed for 11 weeks in the spring of 1957 when adenovirus type 4 was prevalent. 16 cases of disease were found in the vaccinated men instead of the 36 expected, and 4 cases were found by laboratory tests to be due to adenovirus instead of the 24 expected—*i.e.* an effective reduction of 55% and 82% respectively.

The serological studies showed that this vaccine produced poor responses against type 3 virus but good responses against type 4. Both serological and field tests showed that this vaccine (II) was more active against type 4 than was a previous batch of vaccine (I) tested by the same workers. *D. A. J. Tyrrell*

CRAMBLETT, H. G., KASEL, J. A., LANGMACK, Marcia & WILKEN, F. D. **Illnesses in Children infected with an Adenovirus antigenically related to Types 9 and 15.** *Pediatrics.* Springfield, Ill. 1960, May, v. 25, No. 5, Pt. 1, 822–8.

5 children aged 1½ to 8 years were in hospital on account of non-respiratory illnesses and were in close contact with each other. They became ill during the course of 2 weeks. The most prominent manifestations were fever, cough, rhinorrhoea and erythema of the pharynx, but there were also pulmonary rales and rhonchi, vomiting and diarrhoea. The incubation period was probably about 4 days.

A virus was isolated from the throat or faeces of all five. Paired sera were available from 4 children and antibody rises against the virus were shown in each of these. There were no virus isolations and no antibodies were detected in specimens from 8 other children who were in the ward at the time and who did not have an illness of this type.

A virus was neutralized by a type-specific immune serum against adenovirus type 15 and not against type 9 and the virus haemagglutinin was inhibited by an antiserum against adenovirus type 9 and not against type 15. The haemagglutinin was active against human and rat red cells and thus resembled the haemagglutinin of prototype adenovirus type 9 and not type 15. Some patients showed antibody rises against types 9 and 15.

The authors conclude that the data suggest but do not prove that the virus isolated caused the illnesses observed. [ROSEN (this *Bulletin*, 1960, v. 35, 615) seems to have encountered strains similar to these but finds in general very close agreement between neutralization and haemagglutination inhibition and few cross reactions.] *D. A. J. Tyrrell*

SANDIFORD, B. R. **Virological Investigations into Epidemic Bronchiolitis of Infants.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, May, v. 19, 74–8. [10 refs.]

64 pairs of throat swabs, 43 faecal and 15 lung juice specimens, and 54 paired sera (or second sera in a few cases) were collected from 73 infants under 2 years of age who were admitted to Dudley Road Hospital, Birmingham, during the winter of 1956–57 with acute bronchiolitis. Specimens of lung tissue, lung juice and tracheal secretion were also collected at autopsy from 8 of these infants. No virus was isolated by amniotic passage in 10-day-old chick embryos, but adenovirus Type 1 was isolated in HeLa cells from the faeces of 4 patients and from the throat swabs of 2 others. Also ECHO virus Type 12 and another virus, not identified, were isolated in amnion cells from 2 other patients. A 4-fold rise in antibody was demonstrated in 1 of the 6 patients from whom adenovirus was isolated. No causal relationship between adenovirus Type 1 infection and acute bronchiolitis was shown. *D. Taylor-Robinson*

SCHULTZ, I., FRIEDMAN, M. & PIERCE, W. E. **Relationship of Adenoviruses to Respiratory Illness in Ten Naval Recruits sampled repeatedly during Training.** *Amer. J. Hyg.* 1960, Mar., v. 71, No. 2, 141–6, 1 fig. [12 refs.]

A diagnostic 4-fold antibody rise to Type 4 adenovirus was observed in at least 1 test (complement-fixation, neutralization or haemagglutination-inhibition) with sera from 6 of 10 recruits who were selected at random at the Naval Training Center, Great Lakes, Illinois, and studied daily over a 7-week period. From 4 recruits showing antibody rise, Type 4 adenovirus was isolated in HeLa cell culture. However, the authors point out that adenovirus infection cannot be held responsible for the majority of complaints reported since (i) the highest incidence of symptoms was reported up to the 5th week while virus isolations were made in the 4th and 5th weeks and antibody rise occurred after the 4th week (except in 1 case), and (ii) although most men complained of at least 1 symptom on most days of the study, at the time of virus isolation symptoms were not increased and consisted mainly of nasal stuffiness or discharge and cough without fever, *i.e.* symptoms ordinarily classified as "common cold". *D. Taylor-Robinson*

SUZUKI, S., TATENO, I., KITAMOTO, O. & SUGIURA, S. **The Role of Adenoviruses as the Etiological Agent of Sporadic Acute Respiratory Infections especially that of "Virus Pneumonia" in a Civilian Population.** *Japanese J. Exper. Med.* 1959, Dec., v. 29, No. 6, 601–13, 4 figs. (1 on 2 pls.) [Numerous refs.]

"The role of adenoviruses as the etiological agents in the acute respiratory infections of a civilian population was studied over a period of 2 years and it was found to be responsible for only about 2–4% of the adult cases.

"Extensive efforts were made to find out cases of virus pneumonia due to adenovirus and 4 definite and 8 suspected cases were found out of 142 cases of the so-called 'virus pneumonia'. The incidence of developing pneumonia upon infection with adenovirus appeared to be larger in younger children than in adults."

TENG, Chin-Hsien. **Adenovirus Pneumonia Epidemic among Peking Infants and Preschool Children in 1958.** *Chinese Med. J.* Peking. 1960, Apr., v. 80, No. 4, 331–9, 5 figs. on 2 pls.

An epidemic of bronchopneumonia occurred in Peking (and probably elsewhere in Northern China) between October 1958 and February 1959. This paper presents a readable account of a combined study conducted in several Peking hospitals. The patients were mostly aged 6 months to 2 years and presented with bronchiolitis and severe anoxaemia, often followed by congestive heart failure. The leucocyte count was not raised and pathogenic bacteria were not usually isolated. An epidemiological survey showed that in 1 area 14·2% of children under the age of 2 had the disease. The overall mortality was 16% but reached 33·6% in a group of 535 "very serious" cases. In fatal cases death occurred in the second week of disease and other patients began to recover at about this time. A great many methods of treatment were used including "traditional drugs and acupuncture", 7 antibiotics, digitalis, intravenous glucose and blood or plasma. Digitalis and intravenous fluids were thought to be effective but antibiotics failed to control the infection. The lungs of fatal cases showed necrotic and proliferative bronchitis and peribronchial pneumonia and in some cases intranuclear inclusions were found like those produced by adenoviruses [this *Bulletin*, 1958, v. 33, 929].

Adenoviruses of types 3 or 7 were isolated from 70·4% of 81 specimens tested; adenovirus complement-fixing antibodies were found in the sera of 66·9% of cases (control groups showed 21·4% and 5·3%) and a few antibody rises were detected. It was concluded "that adenovirus was chiefly responsible for the epidemic".

D. A. J. Tyrrell

NÁSZ, I. & TÓTH, M. Nachweis von komplementbindenden und neutralisierenden Antikörpern gegen Adenoviren. [**Demonstration of Complement Fixing and Neutralising Antibodies against Adenoviruses**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 2, 141–8. [16 refs.]

An investigation of the occurrence of antibodies adenoviruses in persons living in Hungary was carr out on 748 sera by the complement-fixation test and 148 sera by the neutralization test. Complement-fixi antibody in titres of 4 or greater was found in 268 of 6 (42·4%) sera from patients suffering from non-respirat diseases, and in 56 of 116 (48·2%) sera from patie suffering from acute respiratory infections. In the neut lization tests, which were carried out with types 1 antigens mainly on sera containing complement-fixi antibody, 19·5% of sera contained antibody to a sin type of adenovirus, 18·2% to 2 types, and 16–17% c tained antibody to 3, 4 or 5 types. *D. J. Baue*

BATTISTINI, A. & SERRA, C. Comportamento degli an corpi fissanti il complemento verso gli adenovir in soggetti appartenenti a vari gruppi di età. [**B haviour of Complement Fixing Antibodies Adenoviruses in Subjects belonging to Vario Age-Groups**] *Ann. Sclavo.* Siena. 1960, Mar.–Ap v. 2, No. 2, 109–22, 2 figs. [28 refs.]

The English summary appended to the paper is follows:—

"The authors have studied the behaviour of comp ment-fixing antibodies to adenoviruses in different grou examining samples of serum of 330 individuals betwe 0 days and 15 years of age. The antibodies present 100% of the cases at birth (blood from umbilical co are still detectable in a high percentage (93·3%) in t first month of life; they decrease later till reaching t lowest values between the second and sixth month age; thereafter the authors remarked a gradual increa which brought to 50% the positivity in the groups 2- 3–4, 4–5 years of age.

"Even higher percentages were found in the grou from 5–10 and 10–15 years of age (63·3% and 60%, spectively). In the umbilical cord blood, the antibody ra was sometimes higher than in the corresponding moth blood."

OLAKOWSKI, T. **The Epidemiological Significance Recurring Jaundice.** *J. Hyg., Epidemiol., Micr biol. & Immunol.* Prague. 1959, v. 3, No. 4, 39 404, 8 figs. [34 refs.]

Since 1949 the incidence of infectious hepatitis Czechoslovakia has been high. Among a total of 11,7 adults admitted to hospital with this disease from 19 to 1957, 465 cases of recurring jaundice were observe as well as 30 recurrent cases among 3,157 children a mitted in 1954 and 1955. The percentage of cases repeated jaundice among adults increased during t period to a peak of 5·2% in 1956. The interval betwe the first and second illnesses was over a year in 3 patients, over 5 years in 112, and over 10 years in The peak age incidence of recurrent jaundice was 25– years; among children the incidence was much low than in adults.

In 66 patients specially studied, all had been w between the attacks, which were spaced at intervals ov

1 year. In 6 of these there had been contact with the infection in both illnesses, and in 10 of them in the second illness only. In 22 the clinical manifestations prior to the recurrence of jaundice were similar to those of the prodromal stage of infectious hepatitis. There was no evidence in any of the cases that serum hepatitis might be the cause of the recurrent jaundice. It was impossible to ascertain, in the absence of virological isolations, whether recurrence was due to re-activation of a latent focus or to re-infection with the same or a homologous virus as a result of incomplete immunity following the first attack. *H. Stanley Banks*

Segal', L. S. & Kulinich, I. M. **Comparative Assessment of some Laboratory Methods for the Diagnosis of Infective Hepatitis. I. Study of the Diagnostic Value of the AVB and the Heterohaemagglutination Reactions.** *Problems of Virology.* London. 1959, v. 4, No. 3, 70–73. [Translated from Russian.]

Vanikar, V. A. & Bhatt, J. T. **Serum Glutamic Oxaloacetic Transaminase Activity and Serum Glutamic Pyruvic Transaminase Activity in Liver Diseases.** *Indian J. Med. Sci.* 1960, Apr., v. 14, No. 4, 344–50, 2 figs.

The authors have investigated the use of estimating serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) in liver diseases. They found that although some rise in level can be seen in obstructive jaundice, it is much less than that in hepatocellular jaundice. Thus the quantitative estimation of these enzymes can help in distinguishing between the 2 conditions. In chronic biliary and portal cirrhosis, and in chronic hepatitis, and transaminase levels are sometimes normal or only little raised. The highest levels were seen in acute hepatitis and it was noticeable that in this condition the transaminase level was the last of several liver function tests to return to normal. Measurement of the transaminase levels was particularly useful in hepatitis or in cirrhosis when sudden rises indicated a fresh onset of liver damage.
H. Lehmann

Bodansky, O., Schwartz, M. K., Krugman, S., Giles, Joan P. & Jacobs, A. M. **Comparison of Activities of Isocitric Dehydrogenase and Glutamic-Oxalacetic Transaminase in Serum in Infectious Hepatitis.** *Pediatrics.* Springfield, Ill. 1960, May, v. 25, No. 5, Pt. 1, 807–11, 1 fig.

Isocitric dehydrogenase is normally present in human serum but its concentration is raised specifically in patients with liver disease, particularly in acute hepatitis. The present investigation was undertaken to follow the changes of the enzyme activity in the serum of children who develop hepatitis, and to compare it with those of the glutamic-oxalacetic transaminase. This latter enzyme is well known to be raised in liver disease and also specifically in hepatitis.

42 subjects were examined at the Willowbrook State School, Staten Island, New York. 9 patients received 1 ml. of serum subcutaneously from a patient who had previously had hepatitis at the Institution, and they were compared with 5 control subjects. Others were given infective material in various ways and control subjects were given the virus as well as a gamma-globulin preparation. In 9 patients who developed clear clinical evidence of the disease maximum values for both enzymes were attained on the same day but the relative rise in glutamic-oxalacetic transaminase was much greater. The authors consider that there is no advantage in determining the isocitric dehydrogenase. *H. Lehmann*

Sutorý, K. & Hendrich, F. Naše zkušenosti se sledováním aktivity sérové cholinesterázy u hepatopatií. [**Our Experience Investigating the Serum Cholinesterase Activity in Hepatopathies**] *Časopis Lékařů Českých.* Prague. 1960, June 3, v. 99, No. 23, 711–16. [24 refs.]

The English summary appended to the paper is as follows:—

"The authors investigated the serum choline esterase activity in a group of 70 healthy and 92 sick individuals, using the titration method as modified by Kommerell and Franken with special attention to different types of hepatopathies. The results obtained hitherto provide evidence that estimations of the serum choline esterase activity are suitable for the detection and diagnosis of disturbances of the liver parenchyma. The authors stress in particular the significance of this test in dynamic investigations in infectious hepatitis, where the early drop of the serum choline esterase activity contributes to an early diagnosis. The values of the serum choline esterase activity usually correspond to the clinical picture and justify prognostic conclusions; frequently the values, however, do not run parallel with the thymol turbidity test. The authors draw attention to the advantages and disadvantages of the method."

Märki, H. H. & Wick, A. Zur Beeinflussung von Bluteiweiss- und weissem Blutzelbild durch die Leber bei der Hepatitis (Hepatitis epidemica und Serumicterus). [**Hepatic Influence on Blood Proteins and Lecucocytes in Hepatitis**] *Schweiz. med. Woch.* 1960, June 11, v. 90, No. 24, 657–61. [Numerous refs.]

Wahi, P. N., Ramachandran, S. & Kehar, U. **Adrenal Cortical Function in Infectious Hepatitis.** *Indian J. Med. Sci.* 1960, Apr., v. 14, No. 4, 302–7, 2 figs. [25 refs.]

It is known that infections can lower the suprarenal functions but little has been contributed to the subject as regards the effect of infective hepatitis on the adrenal cortex. This paper presents results of suprarenal function tests on 46 patients with infective hepatitis admitted to the wards of the S.N. Medical College Hospital in

Agra, India. Most of the tests were concerned with the response of the patient to the injection of corticotrophin: rise in urinary uric-acid/creatinine ratio; fall in serum cholesterol, rise in urinary 17-hydroxycorticosteroid excretion, fall in circulating eosinophils. In addition 24-hour urinary excretion of 17-hydroxycorticosteroids, of urinary uropepsin, and of urinary 17-ketosteroids was determined. Lastly, the serum sodium level was measured.

In a significant proportion of the 46 patients, the number varying from 13–37 in the different tests, subnormal results were obtained. This may be due to the inadequate destruction of suprarenal hormones in liver disease with a resultant compensatory atrophy of the adrenal cortex or due to a primary damage of this organ.

H. Lehmann

RASKA, K. & RADKOVSKÝ, J. **Comparative Epidemiological Study in Infectious Hepatitis and Poliomyelitis.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 4, 365–81, 10 figs. [12 refs.]

An epidemiological study was made of infectious hepatitis and poliomyelitis during the period 1950–58 in 653 villages and towns in Czechoslovakia. The mean morbidity rate for infectious hepatitis was 290 cases per 100,000 population per year, and for poliomyelitis 7 cases per 100,000 population per year, a ratio of 42:1. The clinical manifestation rate of infectious hepatitis is therefore far higher than that of poliomyelitis. Infectious hepatitis spreads more slowly than poliomyelitis and its seasonal incidence is later; small outbreaks occur most often in schools and other communities, and the total morbidity is less in villages than in small towns. These epidemiological features of infectious hepatitis are mainly due to its longer period of incubation and shorter period of excretion of the virus than in poliomyelitis.

H. Stanley Banks

CAJAL, N., ADERCA, I., IANCONESCU, M., OPRESCU, Elena, DANIELESCU, Geta & BÎRCĂ, A. Incidența anticorpilor antipoliomielitici la copiii din Republica Populară Romînă. [**The Incidence of Poliomyelitis Antibodies in Children in the R.P.R.**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, Jan.–Feb., v. 5, No. 1, 47–54, 8 figs.

An investigation has been made of the occurrence of poliomyelitis neutralizing antibody in the sera of 111 children living in Bucharest and of 108 living in 3 rural areas in Rumania. Antibody to at least 1 type of poliomyelitis virus was present in 187 sera (85·3%); the number of sera containing antibody was at a minimum between 7 and 12 months of age, and then rose to attain a maximum in children aged 13–15 years. Of the 187 sera with antibody, 63 (33·6%) contained antibody to all 3 types, 67 (35·8%) to 2 types and 57 (30·4%) to a single type. Type 1 antibody predominated in the sera of children living in Bucharest, and types 2 and 3 in the children living in the rural areas. *D. J. Bauer*

GRANICKI, O. Choroba Heinego-Medina na Śląsku latach 1951–1956. [**Poliomyelitis in Silesia duri the Years 1951–1956**] *Przegląd Epidemiol.* Warsa 1959, v. 13, No. 4, 325–37, 6 figs. English summa (6 lines).

Between 1951 and 1956 1,411 patients with poliomy litis were treated in the Infectious Diseases Hospital Bytom, Silesia. The usual seasonal trend in inciden was observed with a maximum in August or Septemb Children aged 2 years were mainly affected (305 cases 1953–56). In 1,328 of 1,380 cases (96.2%) the disease to the paralytic form, and the location of the paralysis given in detail in tables. Among 1,243 patients there w paralysis of 1 limb in 603, 2 limbs in 402, 3 limbs in and 4 limbs in 169. The course of the disease was ve mild in 174 of 1,445 patients, mild in 209, moderate 353, severe in 314, very severe in 330, and fatal in 6 25 fatal cases occurred in the 2–3-year age-group.

D. J. Bauer

WILLIAMS, H. C. M. & MCLACHLAN, I. M. **A Wint Outbreak of Poliomyelitis, Southampton, 195 59.** *Med. Officer.* 1960, Apr. 29, v. 103, No. 1 253–5, 1 fig.

The epidemic began with 4 cases in October follow by 15, 19, 23 and 8 cases in the 4 following months. did not appear to spread outside the borough. Two-thir of the cases were paralytic and of 18 patients over t age of 21 as many as 12 suffered from respiratory par lysis. 5 deaths occurred in the 61 paralytic cases ages 3 weeks and 12, 24, 28 and 30 years).

Multiple cases in schools were infrequent; there we 5 instances of 2 cases in the same home. 18 patients ha received poliomyelitis vaccine but vaccination was co tinued throughout the outbreak and only half of the had received 2 injections 2 months or more before t onset of their illness. *A. Bradford Hill*

SIEDLER, H. D., KALTER, S. S., THRUPP, L. D., UTZ, J. FINUCANE, D. L. & PARROTT, R. H. **Outbreak Type 3 Paralytic Poliomyelitis in Washingto D.C., in 1957.** *Amer. J. Hyg.* 1960, Jan., v. 7 No. 1, 29–44, 7 figs. [30 refs.]

The epidemiological pattern of an outbreak of paraly poliomyelitis and concurrently of aseptic meningitis du ing the summer of 1957 in Washington D.C. and t surrounding district is described. Among the city cas Negro pre-school children from low income household were selectively attacked with the paralytic disease, a this was correlated with a low vaccination rate in th age-group and socio-economic group. This segment the population in cities is likely to be subject to relative high risk in outbreaks of poliomyelitis. Out of 70 poli virus isolations from all sources in this outbreak, no le than 65 were of type 3 poliovirus, 3 were of type 2, a 2 were of type 1. The predominance of type 3 is u usual; no correlation was found between the virus ty and the clinical characteristics. The majority of t cases of aseptic meningitis in the city group were believ

be associated with type 3 poliovirus infection, but in he county areas only 1 poliovirus was found in 11 virus solations; the remainder were a miscellaneous group omprising Coxsackie viruses A9, B3, B4 and B5 and ECHO viruses 6 and 9. *H. Stanley Banks*

GILLERT, K. E., GRÜTZNER, L. & HARTMANN, H. Über neutralisierende Antikörper vor und nach der Impfung gegen Poliomyelitis mit Salkimpfstoff. **[Neutralizing Antibodies before and after Vaccination against Poliomyelitis with Salk Vaccine]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 3, 289–98, 4 figs. [16 refs.]

The authors have investigated the development of poliomyelitis neutralizing antibody in 453 sera from 171 children vaccinated with Salk-type poliomyelitis vaccine n Germany. 39 persons aged 1–13 years who had no ntibody before vaccination had all formed type II antiody after receiving 2 doses of vaccine, whereas 7 and 10 ad not formed antibodies to types I and III respectively. The mean titre of type II antibody was 32, and titres of 512 or higher were observed in a few instances. In 145 children who had antibody before vaccination 15 (10.3%) ad not formed type I antibody 14 days after the 2nd dose f vaccine, and 3 (2·1%) lacked type II and 18 (12·4%) ype III antibody. In 82 children examined 14 days after he 3rd dose of vaccine type I antibody was still absent n 4, type II in 2 and type III in 4; the remainder showed itres of 128 to types I and II virus and somewhat lower itres to type III. *D. J. Bauer*

MARTINS DA SILVA, M., LÓPEZ BERRIOS, M. & ALCOCER, J. J. **The Use of Attenuated Poliovirus in an Epidemic Area, Managua, Nicaragua, 1958.** *Amer. J. Hyg.* 1960, Mar., v. 71, No. 2, 179–92, 5 figs.

Every year since 1938 cases of poliomyelitis have been reported in Nicaragua. In 1958 there was an epidemic involving 238 cases and 17 deaths, starting at the end of May and terminating at the beginning of November with the peak incidence in the first week in August. 87% of the patients were under 3 years of age. The main brunt of the disease was borne by the department of Managua. As a result of a call for help to the Pan American Sanitary Bureau the senior author visited Managua in early August, to determine the type of poliovirus responsible for the epidemic and to help organize a vaccination programme with attenuated poliovirus. The epidemic was due to type 2. Starting on 5th September, 1958, 42,119 children (80% of the age-group 2 months to 10 years) in Managua city were vaccinated orally with $10^{4.9}$ TCD50 of type 2 poliovirus in 12 days. At intervals of 3 weeks thereafter types 3 ($10^{5.2}$ TCD50) and 1 ($10^{4.7}$ TCD50) were administered.

Later the campaign was extended to outlying communities and a scheme for vaccinating the newborn was instituted. Newborn infants now receive 2 ml. of trivalent vaccine containing $10^{6.1}$ of each type of virus. The epidemic had subsided by the time the vaccine programme had been started. No illness attributable to vaccination was recorded. In the 8 months following the completion of the mass vaccination campaign there have been no cases of paralytic poliomyelitis in Managua. A similar period of freedom from the disease has not occurred for over 8 years [this could be due to the vaccination campaign or to the epidemic]. 74%, 58% and 80% of a small group of children without antibodies to types 1, 2 and 3 respectively had acquired them some time after vaccination.

The ease of administration, especially in using trivalent vaccine, is stressed. *A. J. Beale*

GIBINSKI, K., MAKOWER, H., SKURSKA, Zofia, BARA, B. & SYPUŁOWA, Alicja. **Bornholm Disease in Upper Silesia.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 421–9, 2 figs. [16 refs.]

This paper is an account of several outbreaks of Bornholm disease in Poland (Upper Silesia). During the years 1954–56 37 of 64 subjects with a clinical diagnosis of Bornholm disease were examined for the presence of viruses. 9 strains were isolated in 1954 but could not be identified. In 1956 all the viruses proved to be Coxsackie A4 and were pathogenic for suckling mice. In 1957 there was an epidemic of Bornholm disease and 15 strains were isolated from 45 patients; all were isolated in HeLa cells, none directly in newborn mice. These strains proved to be Coxsackie B3. There is a full account of the epidemic and of the clinical features. The chief characteristics of Bornholm disease are: (1) the sudden onset of symptoms, particularly severe pain; (2) slight or negative laboratory findings; and (3) the short and favourable course of the disease, although relapses do sometimes occur. *A. J. Beale*

PARKER, W., WILT, J. C., DAWSON, J. W. & STACKIW, W. **Landry-Guillain-Barré Syndrome—the Isolation of an Echovirus Type 6.** *Canadian Med. Ass. J.* 1960, Apr. 16, v. 82, No. 16, 813–15, 1 fig. [11 refs.]

This paper presents a full clinical history of a case of Landry-Guillain-Barré syndrome. ECHO virus type 6 was isolated from the faeces and from the cerebrospinal fluid of the patient. The patient had only low titre antibodies to ECHO 6 virus in the acute and convalescent serum samples but also had only low titre antibodies to type 1 poliovirus and to herpes simplex virus. Electrophoretic analysis of the serum proteins revealed that the content of gamma globulin was below normal and the alpha-1 globulins were absent. It is concluded that the illness was due to ECHO 6 virus and that perhaps the alpha-1 globulins are concerned with the immunity to virus diseases. This last possibility is being further investigated. *A. J. Beale*

GRAY, J. E. **Rubella in Pregnancy. A Report on Six Embryos.** *Brit. Med. J.* 1960, May 7, 1388–90, 13 figs. on 2 pls.

This is a useful pathological contribution to the subject of congenital abnormalities following maternal rubella in

the first trimester of pregnancy. The 6 pregnancies were terminated by hysterotomy or hysterectomy as a consequence of rubella contracted in the 2nd to 9th week of pregnancy. Histology showed definite lesions in the eyes, ears, or heart of 3 of the 6 foetuses, and an abnormality was suspected in a 4th. The lesions appeared to be the result of cell destruction such as is caused by virus action in tissue culture. They are beautifully illustrated.

[Such studies are a contribution to prospective investigation of the frequency of congenital abnormalities following maternal rubella.] *H. Stanley Banks*

SWAIN, R. H. A. **The Nature of the Newcastle Agglutinin in Infectious Mononucleosis and Infective Hepatitis.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 67–80. [30 refs.]

A study has been made of the properties of the substance present in the sera of patients suffering from infectious mononucleosis which will agglutinate human red cells previously treated with Newcastle disease virus [this *Bulletin*, 1947, v. 22, 77] referred to in the present work as Newcastle agglutinin. In titrations of the Newcastle agglutinin content of 83 sera from healthy persons the titres did not exceed 80, and taking this titre as the upper limit of normality positive results were obtained with 77·1% of 105 sera from patients with infectious mononucleosis, 41·6% of 24 sera from patients with infective hepatitis, and 8·2% of 328 sera from patients suffering from other infectious diseases. Newcastle agglutinin was present in low titres in the sera of normal persons of all ages, and also in 12 samples of serum from the umbilical cord; it was also present in the sera of domestic and laboratory animals, particularly high titres being encountered in rabbits. The agglutinin could be distinguished from Forssman antibody by its failure to be absorbed by guineapig kidney and from the heterophil antibody of infectious mononucleosis by its failure to be absorbed by bovine red cells. The agglutinin was also distinct from Newcastle disease neutralizing antibody, from antibodies to a number of other viruses, the Francis and Chu inhibitors and the rheumatic factor. The Newcastle agglutinin is considered to be produced in response to an antigen liberated from the tissues as the result damage occurring during the disease process.

[See also this *Bulletin*, 1951, v. 26, 209 *bis*.]

D. J. Baue

GOTHBERG, L. A. **Severe Infectious Mononucleo treated with Chloroquine Phosphate.** *J. Am Med. Ass.* 1960, May 7, v. 173, No. 1, 53–7, 4 f

"Four patients with infectious mononucleosis, wh cases are described, showed a dramatic, and possi specific, clinical response to treatment with chloroqu (Aralen) phosphate. Although the possible modes action of chloroquine phosphate, as outlined here, not entirely understood, further trial of the drug is w ranted because of (1) the gratifying symptomatic re patients obtained from its use and (2) the light that m be shed on the mechanism of action of the 4-aminoqui lines."

VAN LEEUWEN, G. & BROOKE, C. E. **Oculoglandu Cat-Scratch Disease.** *J. Dis. Children.* Chica 1960, May, v. 99, No. 5, 667–8. [10 refs.]

The oculoglandular syndrome in cat-scratch disease uncommon, judging from the literature [this *Bulle* 1952, v. 27, 426; 1954, v. 29, 157, 812; 1957, v. 32, 3 1958, v. 33, 229, 340 *bis*]. A case history of this fo of the disease in an 11-year-old girl is here present She developed a painless swelling about the left eye a anterior to the left ear. About 30 days before her illn began her face had been clawed by a stray cat. T condition of the girl slowly got worse and after 3 we she was admitted to hospital. On the 3rd day in hospi her temperature rose to 102°F. and the pre-auricular a was fluctuant. Later this area was aspirated on 2 oc sions and sterile pus was removed.

The skin test with cat-scratch antigen was positi The patient made a complete recovery.

"Until recently a patient presenting with the ocu glandular symptom complex was ordinarily thought have tuberculosis, tularaemia, or leptotrichosis. C scratch disease may well prove to be a commoner ca of this complex than previously supposed." The imp tance of early suspicion and diagnosis of cat-scrat disease is stressed. *M. E. Delafield*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

COWAN, S. T. & STEEL, K. J. **A Device for the Identification of Microorganisms.** *Lancet.* 1960, May 28, 1172–3, 2 figs.

In this paper the authors describe a simple mechanical evice which simplifies the comparison of a list of redetermined characters of an unknown bacterium with similar list of characters of known organisms. [With arefully prepared diagnostic tables this device would e of value in a laboratory concerned with the routine dentification of large numbers of bacteria.]

John R. Norris

GREENBERG, B. **Persistence of Bacteria in the Developmental Stages of the Housefly. III. Quantitative Distribution in Prepupae and Pupae.** *Amer. J. Trop. Med. & Hyg.* 1959, Nov., v. 8, No. 6, 613–17, 1 fig. **IV. Infectivity of the Newly Emerged Adult.** *Ibid.*, 618–22, 3 figs. [21 refs.]

II. Mature, actively feeding maggots, when removed rom the breeding medium and starved for a day, usually ose more than 90% of their bacteria. This decline in he number of bacteria is of the same magnitude as the oss sustained by the non-feeding prepupa and it seems kely that the primary causes of this loss in the ousefly prepupa are curtailed feeding and continual limination. These processes in the housefly prepupa educe the bacterial count to 10^5; in the hornfly, however, utosterilization may actually be carried to completion. Dissections of pupae provide evidence for the transocation of the intestinal flora of the prepupa to the nner surface of the puparium, the moulting membrane and the surface of the pupa. The pupal gut retains very few organisms. The fly emerges with a bacterial count of about 10^2.

IV. Quantitative bacteriological studies of faeces and meconium of flies reared with a single species of a human pathogen, cumulative sampling of faeces from flies maintained aseptically for 2 days and sampling the digestive tract give results which indicate that the fly's gut contains but few bacteria. Once, however, the fly takes to wing the number and kinds of micro-organisms it acquires depends on the material available to it on its flights. [See also this *Bulletin*, 1960, v. 35, 75.]

H. J. Bensted

HAENEL, H. Aspekte der mikroökologischen Beziehungen des Makroorganismus. Mikroorganismen im menschlichen und tierischen Darm und in anderen Organen des Menschen. [**Microorganisms in the Intestinal Tracts of Man and Animals, and in Other Organs of Man**] *Zent. f. Bakt.* I. Abt. Ref. 1960, v. 176, No. 1, 1–121, 40 figs. [350 refs.]

WEIBULL, C. & BECKMAN, H. **Growth of Bacterial L. Forms and Bacterial Protoplasts.** *J. Bacteriology.* 1960, May, v. 79, No. 5, 638–49, 5 figs. [Numerous refs.]

KORNBERG, A. **Biologic Synthesis of Deoxyribonucleic Acid. An Isolated Enzyme Catalyzes Synthesis of this Nucleic Acid in Response to Directions from Pre-Existing DNA.** *Science.* 1960, May 20, v. 131, 1503–8, 8 figs. [Numerous refs.]

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Colicines; Other Therapeutic Substances; Disinfection.**

'ARI, A. Contribution à l'étude de l'action des antibiotiques sur l'immunité. [**Contribution to the Study of the Action of Antibiotics on Immunity**] *Ann. Inst. Pasteur.* 1959, Nov., v. 97, No. 5, Suppl., 87 pp., 1 fig. [392 refs.]

This long paper from the Therapeutic Chemistry Department of the Institut Pasteur is in 2 parts. The first is a review of the literature of the failure of animals or patients treated for bacterial infections with antibiotics or sulphonamides to develop the degree of immunity

which usually accompanies recovery, as evidenced clinically by subsequent relapse or low antibody titres, or experimentally by susceptibility to reinfection.

The second part gives an account of the author's own work, for the most part hitherto unpublished, directed to determining the importance of three possible mechanisms underlying this phenomenon.

(1) An effect of the antibiotic on the host. In some experiments, very briefly reported, it was found that administering chloramphenicol to rabbits somewhat reduced the amounts of antibody formed in response to various antigens (no other antibiotic was studied, and the author appears not to attach much importance to this finding).

(2) An effect of the antibiotic on the antigenic constitution of the infecting organism. It was found that when *Salmonella typhi* was cultivated in medium containing chloramphenicol, the Vi antigen diminished in amount, and agglutinability by O antiserum increased. Animals immunized with a suspension of such organisms yielded serum with a diminished protective action against infection in mice and in chick embryos. The conditions governing this antigenic change were examined in detail: it is rapidly reversible in normal medium.

(3) Reduction in the number of infecting organisms and hence diminished stimulus to antibody formation. The importance of this fairly self-evident explanation was illustrated in experiments of the following kinds. Mice were inoculated with a number of *Salmonella typhi-murium* which killed a proportion of controls and a group was treated with tetracycline, nearly all of which survived. All animals were re-inoculated 14 days later with a large multiple of a lethal dose. Only 4% of previously treated mice survived, but 50% of controls. In a similar experiment with pneumococci no controls survived, but the mortality on re-inoculation after successful treatment with each of 3 antibiotics was heavy.

Mice were then given 3 doses of a vaccine before inoculation and these and unvaccinated controls were inoculated and divided into groups given and not given antibiotics. When survivors were re-inoculated later the survival rate was much higher in the originally vaccinated animals. In a further series of experiments, with both the organisms mentioned, vaccination was started at the time of first inoculation and the same type of result was regularly produced: the vaccine even lowered the mortality in untreated controls. In connexion with this, instances are cited in which vaccines have been successfully used during the course of acute infections in man, in combination with chemotherapy or even alone.

L. P. Garrod

HINTON, N. A. & ORR, J. H. **The Effect of Combinations of Antibiotics on Coagulase-Positive Staphylococci.** *Canadian Med. Ass. J.* 1960, Feb. 6, v. 82, No. 6, 311–14, 1 fig.

These experiments were done with 66 strains of staphylococci obtained from 4 different hospitals (2 in Kingston, Ontario, and 1 each in Toronto and Montreal) in order to obtain as wide a variety as possible: their phage types were determined but these are not given, nor is it actually stated that they were all different. All were sensitive to the antibiotics used. Tests of combin action were made by 2 agar diffusion methods; that which filter paper strips containing different antibioti are laid on a plate at right angles crossing one anoth and that in which one antibiotic is contained in t medium in a gradient plate and the second is in a pap strip at a right angle to the gradient. After incubati transfer by velvet pad to a replica plate provided t information about the bactericidal action from whi the result was judged. Findings are given in a Table numbers of strains against which different combinatio showed synergism, addition, indifference or antagonis (the distinction between addition and indifference is n defined). They are given for both methods, including variations of the crossed strip method, the amounts of t antibiotics being adjusted to produce zones of differe widths.

Penicillin + streptomycin, penicillin + bacitracin, a bacitracin + chloramphenicol were synergic again many strains: streptomycin + chloramphenicol a streptomycin + tetracycline showed antagonism again most. The other 4 combinations of these 5 antibioti showed no consistent pattern of behaviour except greater proportion of additive or indifferent effects. Son interesting experiments are described and illustrated which the slope in the gradient plates was varied, and is shown that a shallow gradient elicits antagonism wh a steep one fails to reveal it: this accounts for the fa that the gradient plate method more often revealed th type of effect than the crossed strip method. The latt has the advantage of greater simplicity, and is considere serviceable for routine use.

L. P. Garrod

DRESSLER, J. A. W. **Common Bacteria and their I creasing Drug Resistance.** *Med. Proc.* Johanne burg. 1960, Feb. 13, v. 6, No. 3, 74–7, 1 fig.

This paper from Johannesburg reports the frequenc of sensitivity to 10 antibiotics, sulphonamides and fur dantin in succeeding years from 1954 to 1959 of 1,6 strains each of *Staphylococcus aureus* (coagulase-positive haemolytic streptococci (not grouped or otherwise furth identified), coliform bacilli (" the whole of the coliform aerobacter group") and *Proteus* spp. These were isolate from clinical material in the years specified and teste by a disc method. The results are presented both tables and in a diagram. The general trend found towards increasing resistance, particularly in staphyl cocci to most of the agents, and (in all organisms) sulphonamides and the 3 tetracyclines. On the basis these findings the " drugs of choice " are considered be for staphylococci, Kantrex (kanamycin) erythromyc and novobiocin; for streptococci, furadantin, erythr mycin and chloramphenicol; for both coliform bacilli a *Proteus*, kanamycin. Other antibiotics included are pe cillin, streptomycin and neomycin. [There are points interest in these extensive findings rather detracted fro by lack of identification of the bacteria studied. T choice of kanamycin for treating 3 of the 4 types of i fection calls for a serious warning. The author hims says: " Neomycin is excellent, but because of its toxici is used only for topical application ". Kanamycin

closely related to neomycin and can have the same toxic effects, notably on the 8th nerve, even though its liability to cause these is claimed to be less than that of neomycin: a parenteral course of either should be short and given only to patients with adequate renal function.]

L. P. Garrod

SENECA, H., ZINSSER, H. H. & LATTIMER, J. K. **Relation of Drug Resistance to Enzyme Activity among Coliform Bacteria. New Approach to Problem.** *J. Amer. Med. Ass.* 1960, Mar. 5, v. 172, No. 10, 1015–18, 1 fig.

These authors have collected strains of *Proteus, Klebsiella, Pseudomonas, Salmonella, Shigella, Escherichia* and *Vibrio*, tested their sensitivity to nitrofurantoin, sulphadiazine, tetracycline, chloramphenicol, erythromycin and an equal mixture of penicillin and streptomycin, and determined their capacity to ferment urea and utilize citrate. They point out that species which form urease and utilize citrate are generally more resistant to these drugs, and suggest that the 2 properties are causally related, in the sense that an organism capable of utilizing simple substrates should be more adaptable.

L. P. Garrod

DOBBERSTEIN, H. Untersuchungen über die Empfindlichmachung antibiotikaresistenter Bakterien. **[Studies on the Restoration of Sensitivity to Antibiotic-Resistant Bacteria]** *Zent. f. Bakt.* II. Abt. 1959, v. 113, Nos. 1/5, 53–9, 3 figs. [15 refs.]

An antibiotic-resistant organism may be rendered sensitive either by a second substance exerting an adjuvant effect (cobalt is cited as a possible example) or by genetic change. These authors briefly review previous observations bearing on the second of these mechanisms, including the work of VOUREKA [this *Bulletin*, 1948, v. 23, 439], studies of the Welsch phenomenon, and experiments in which the change from resistance to sensitivity or *vice versa* has undoubtedly been produced by the provision of desoxyribonucleic acid from another strain. The author then gives the results of some experiments of his own, but without technical details of how they were done, in which protein or nucleoprotein from a sensitive organism restored sensitivity to a streptomycin-resistant pneumococcus.

L. P. Garrod

KIRSHBAUM, A., KRAMER, J. & ARRET, B. **The Assay and Control of Antibiotic Discs.** *Antibiotics & Chemotherapy.* New York. 1960, Apr., v. 10, No. 4, 249–58, 2 figs.

This paper is from the Department of Health, Washington, and explains how antibiotic discs are tested there, giving the composition of the culture media used, the species and strain designations of the test organisms, and details of the performance of the test itself. This consists essentially of comparing inhibition zone sizes in plates seeded with an appropriate test organism produced by the disc under test and by standard discs containing 5 different quantities of the antibiotic (differences slightly less than 2-fold). A standard curve is plotted from the averaged zone diameters produced by 3 each of the standard discs, and on this is read off the quantity in the unknown as indicated by the averaged zone diameters of 6 discs. This should lie between 67 and 150% of the stated content. This method is preferred to the extraction method recommended by others, because it is a test of performance: instances are cited in which discs containing the stated amount of antibiotic failed to produce inhibition zones of corresponding size because its release was affected by the solvent used for it in preparing the disc.

L. P. Garrod

SURGEN, R. C. & NIELSEN, Jean K. **Some Factors influencing the Toxicity (Safety) Test for Antibiotics.** *Antibiotics & Chemotherapy.* New York. 1960, Mar., v. 10, No. 3, 169–73.

This paper is from the Food and Drug Administration, Washington, and begins by explaining that in the United States antibiotics have to be submitted to a safety test. The dose administered is such as to cause no fatalities if the material is of "acceptable purity": the test is therefore really one for impurities. It consists of administering a single intravenous injection of a solution to groups of mice in a volume of 0·5 ml., injected at the rate of 0·1 ml. per second, timed with a metronome. These authors have observed that doses of penicillin and streptomycin which cause no fatalities when dissolved in saline cause a few when dissolved in distilled water: another paper is quoted which reported that procaine penicillin is particularly lethal when dissolved in water (NIR-GROSFELD *et al., J. Pharm. & Pharmacol.*, 1958, v. 10, 253). Actual determinations of the LD50 of tetracyclines in the 2 solvents showed all to be less lethal in saline. It was also found that when the same quantity of antibiotic (1 mgm. chlortetracycline hydrochloride or 1,000 units procaine penicillin G) was administered in 0·25, 0·5, 0·75 or 1 ml., the smaller volumes caused only "mild reactions", 0·75 ml. caused "severe spasms" and some deaths, and 1 ml. caused "very severe spasms" and death of all mice. 0·5 ml. of water alone had no effect but larger volumes up to 1·5 ml. caused spasms and death. [0·5 ml. to a 20 gm. mouse is equivalent to about 1½ litres for an average man: the idea of injecting this volume of distilled water in 5 seconds is appalling. The mere volume must in any case overburden the right heart, but if the fluid is water its hypotonicity must have other effects, including presumably intravascular haemolysis. Such possibilities are not discussed in the paper, which also does not attempt to explain the "spasms" observed or refer to any autopsy findings. It is only surprising that 0·5 ml. of water alone should have been tolerated, the added insult of an antibiotic being necessary to cause fatalities. It is difficult to understand why the use of an isotonic solution was not made a requirement for this test when it was first introduced.]

L. P. Garrod

MURRAY, R. G. E., FRANCOMBE, W. H. & MAYALL, B. H. **The Effect of Penicillin on the Structure of Staphylococcal Cell Walls.** *Canadian J. Microbiol.* Ottawa. 1959, Dec., v. 5 No. 6, 641–8, 14 figs. on 6 pls. [23 refs.]

Penicillin-sensitive staphylococci were exposed to 20 μgm./ml. penicillin for 1–24 hours, fixed in osmium tetroxide, dehydrated, embedded in methacrylate and sectioned, the sections being examined and photographed with an electron microscope. The cells were found to be enlarged, with thin walls and deformities of the "septum" which forms before division: many excellent photographs contrast these changes with the appearance of normal cells. It was thus confirmed visually that penicillin interferes with the synthesis of new cell wall material. A resistant strain exposed to concentrations of penicillin up to 1,000 μgm./ml. did not show these changes: what was said to be a resistant variant of a sensitive strain did so. In the longer term experiments (>3 hours) 0·3M sucrose was added to the medium to prevent lysis, and the appearances were somewhat different: the cell wall was thin, but no septa, either normal or abnormal, could be seen. *L. P. Garrod*

HAMBURGER, M. & CARLETON, Judith. **Bactericidal Action of Penicillin and Tetracycline against Gram-Positive Cocci. In Broth and in Blood Clots, with a Few Observations concerning "Persisters".** *Arch. Intern. Med.* 1960, Mar., v. 105, No. 3, 372–82, 6 figs. [17 refs.]

Fresh human blood was added to bacteria in a tube: when the clot had formed and retracted it was placed in a tube of broth with or without antibiotic and incubated for many days, fresh broth and antibiotic solution being added from time to time to maintain the volume and antibiotic concentrations. One of a batch of such preparations was examined at intervals by removing, washing and grinding the clot and making quantitative cultures from it, penicillin being neutralized with penicillinase and tetracycline with magnesium sulphate. In some experiments clots which had been incubated for 4 days in antibiotic-free broth or broth containing a low concentration of penicillin were then transferred to penicillin broth of low or high concentration. The amount of antibiotic in the clots was also estimated: penetration was adequate, although apparently greater by tetracycline than by penicillin.

It took much longer to kill bacteria within these clots than in plain broth. Since the antibiotic was shown to penetrate the clot, it is surmised that the metabolic state of the bacteria may be responsible for this: they are likened to the "persisters" described by BIGGER [this *Bulletin*, 1945, v. 20, 39]. Pneumococci were killed by penicillin in 3–5 days, but 7 strains of alpha-haemolytic streptococci from cases of endocarditis survived for 12–18 days and a penicillin-sensitive staphylococcus for 9–14 days in different experiments. A small inoculum was more easily killed than a large one. There was little difference in the initial rate of kill achieved by 0·5 and 50 μgm./ml. of penicillin, but the higher concentration was sometimes more effective in eliminating the last f survivors, suggesting that "tapering-off" the clinical d of penicillin may sometimes be inadvisable. Tetracycli tested only against a different strain of staphylococc behaved similarly, taking 15–24 days to sterilize cl containing many organisms, but only 1–3 days for th containing few, whether the concentration of antibio was high or low. *L. P. Garrod*

BRUNNER, R. & PROHASKA, E. Über die Beziehung Penicillinase zur Penicillinresistenz bei *E. co* [**The Role of Penicillinase in Penicillin Resistance of** *E. coli*] *Zent. f. Bakt.* I. Abt. Orig. 19 v. 176, Nos. 7/8, 447–54.

These authors have recently reported that certain io and non-ionic surface-active agents both inactivate penicillinase formed by staphylococci and abolish resistance of these organisms to penicillin when added a culture medium. They have now tested some of the substances (*e.g.* sodium tridecyl-2-sulphate) against pe cillinase formed by strains of *Escherichia coli*, and fou that it too is inactivated, but when the substance is add to a culture medium it has no effect whatever on sensitivity of the penicillinase-forming *E. coli* to penic lin. This may mean that resistance to penicillin in th species is not dependent, as in staphylococci, on enzy formation, but is a distinct and intrinsic property. A other possibility is that intracellular penicillinase in th species is unaffected by these surface-active agents. T presence of the same agents in a medium did not redu the resistance of some strains of *E. coli* and *Prote mirabilis* to tetracycline. [The authors do not state source of their strains of *E. coli*, and how, or inde whether, they identified them. Related organisms mu more often produce penicillinase than does *E. coli* itsel *L. P. Garrod*

MARKOV, K. I. & SAEV, G. K. Die Wirkung des Pen cillins auf die Oxydationsprozesse der penicilli resistenten Staphylokokken. [**The Influence Penicillin on Oxidation Processes in Penicilli Resistant Staphylococci**] *Zent. f. Bakt.* I. Ab Orig. 1959, v. 176, Nos. 7/8, 468–75, 4 figs. [refs.]

These authors from Sofia have previously found [th *Bulletin*, 1957, v. 32, 497, 805] that penicillin and i derivatives can replace thiamine as a growth factor f penicillin-resistant staphylococci. They here describe e periments illustrating the same effect in a different wa These were carried out with penicillinase-forming strai isolated from clinical material. They were cultivated a thiamine-deficient medium, washed and placed in Warburg apparatus with glucose or other substrate, ar thiamine, biotin, penicillin, penicillic acid or penicillo acid. All these substances increased oxygen uptake compared with a control containing none of them about an equal degree. A similar but apparently le pronounced effect was obtained when the substrate w pyruvate or lactate. There is a lag before the stimulatin effect of penicillin appears, whereas that of thiamine

immediate. Previous cultivation on a penicillin-containing medium enhances the effect. *L. P. Garrod*

HILL, E. C. & PHILLIPS, G. O. **The Inactivation of *Bacillus subtilis* Spores in Penicillin by Gamma Radiation.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 8–13, 1 fig. [12 refs.]

A suspension of *Bacillus subtilis* spores was added to a solution of penicillin, which was then freeze-dried, and exposed to a 200 curie ^{60}Co source (1300 rad./min.) for different periods. The penicillin was then dissolved and treated with penicillinase and the surviving spores were counted, in early experiments in plates, and later, because this method gave anomalous results, by a tube dilution method with 10 series of doubled dilutions. Complete sterility was not attained in any test (the fewest survivors being 3·1% after a dose of about 300,000 rads), but the relationship between dose and the numbers of survivors was determined in 3 experiments, and found to correspond closely with the results in 1 experiment in which the spores were irradiated in distilled water. Although environment is known to affect the results of irradiating vegetative bacteria, "it is possible that the spore coat tends to isolate the spore from the environment, which consequently has less effect on the death-rate". *L. P. Garrod*

BATSON, J. M. **Anaphylactoid Reactions to Oral Administration of Penicillin.** *New England J. of Med.* 1960, Mar. 24, v. 262, No. 12, 590–95. [28 refs.]

Much of this paper is a double-page table detailing the features of 26 published cases of reactions to oral penicillin, 2 of which were fatal. 2 further cases treated at the New York Hospital are also recorded. A 15-year-old girl collapsed after swallowing 2 penicillin tablets prescribed by her dentist after an extraction: having previously been given penicillin for pain in the knee and ear-ache. "Interestingly enough, she thought that penicillin was used to relieve pain". She was pulseless and unconscious, but was revived with adrenalin. A 46-year-old man took 2 penicillin tablets for an unstated reason and developed nausea, faintness, sweating, facial oedema and generalized erythema. He responded to diphenhydramine and tripelennamine. *L. P. Garrod*

JOSEPHSON, A. S. **The Development of Antibodies to Penicillin in Rabbits.** *J. Exper. Med.* 1960, May 1, v. 111, No. 5, 611–20, 2 figs. [16 refs.]

Rabbits were given repeated injections of penicillin G mixed with Freund's adjuvant, the initial dose being divided between 20 different subcutaneous sites. Their serum came to contain agglutinin to a titre of 8–128 for red cells previously treated with penicillin G or O. This antibody did not interfere significantly with the action of penicillin on bacteria. Its action on coated red cells was blocked by penicilloic acid but not by penicillamine. Penicilloic acid did not itself produce antibody to penicillin in rabbits. Electrophoresis showed the antibody to be contained in the gamma and beta globulin fractions of the serum: the presence of dextran or albumin was necessary for its action. *L. P. Garrod*

JANSSEN, P. J. **Peripheral Neuritis due to Streptomycin.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 726–8.

"A case of peripheral neuritis due to streptomycin is presented. In cases of peripheral neuritis in patients receiving treatment for tuberculosis, isoniazid is the drug almost certainly blamed, as happened in the present case. The great danger is that the patient who manifests neuritis is considered without further investigation to be "isoniazid-hypersensitive", and the most important and powerful drug is permanently discontinued. In order to avoid this, it is of paramount importance to recognize the real culprit, which may be streptomycin in probably more instances than is realized. A trial with dihydrostreptomycin should be carried out in those cases."

WEISS, C. F., GLAZKO, A. J. & WESTON, Jean K. **Chloramphenicol in the Newborn Infant. A Physiologic Explanation of its Toxicity when given in Excessive Doses.** *New England J. of Med.* 1960, Apr. 21, v. 262, No. 16, 787–94, 5 figs. [38 refs.]

This paper is by members of the staff of Parke, Davis and Co., Detroit. The investigation described was undertaken because of reports of deaths in newborn infants treated with large doses of chloramphenicol. Chloramphenicol in 3 forms, 1 administered orally and 2 by injection, was given to infants of different ages and to older children, and serial assays of the drug in the blood were carried out. From these studies it emerges that in infants 1 or 2 days old the drug is retained in the blood in higher concentrations and for much longer than in older children, regardless of the method of administration. This is attributed to deficient renal tubular function. Evidence was also obtained that the liver is unable to conjugate chloramphenicol wih glucuronic acid to the extent that occurs, *e.g.*, in an anuric adult. It is recommended that the dose should not exceed 50 mgm. per kgm. daily in the newborn full term infant, or 25 mgm. in the premature. [The paper seems to assume that there are regular indications for giving chloramphenicol to the newborn, but the wider question of whether and if so when the antibiotic is indicated at all seems worth considering, in view of the unconvincing reasons for its use mentioned in reports of fatalities.] *L. P. Garrod*

FISHER, M. W. **The Susceptibility of Staphylocccci to Chloramphenicol. A Survey of Experimental and Clinical Experiences.** *Arch. Intern. Med.* 1960, Mar., v. 105, No. 3, 413–23, 1 fig. [78 refs.]

This paper from the Research Laboratories of Parke, Davis and Co., Detroit, endeavours to show that most

staphylococcal infections should be amenable to treatment with chloramphenicol. It first reports some therapeutic experiments in mice: these were inoculated with 8 strains inhibited *in vitro* by 1·6 or 3·1 μgm./ml. and with 16 strains inhibited only by 25, 50 or 100 μgm./ml. The average 50% curative dose for infections by the first group was 28 mgm./kgm. and for the second 95 mgm./kgm., which suggests that the drug is more effective *in vivo* than *in vitro*, and that an increased dosage in man should control infections by a resistant strain. Some *in vitro* tests are then reported with 23 highly resistant strains collected from other investigators: these were tested by both a tube dilution method and with discs, and recommendations are made about how such tests should be done, with emphasis on the use of a small inoculum. Infection with the 2 most resistant of these strains in mice was amenable to chloramphenicol treatment (no details given).

The author then reviews the literature on chloramphenicol resistance in staphylococci, and constructs a diagram showing that its frequency did not increase between 1950 and 1958 and that it appears to be no more frequent in hospitals using chloramphenicol freely than in those where its use is restricted. Most authors have found that Type 80/81, which is frequently resistant to other antibiotics, is almost invariably sensitive to chloramphenicol. Finally it is suggested that the rarity of resistant strains is due not only to the difficulty with which resistance is acquired, but to frequent back-mutation to sensitivity.

L. P. Garrod

Daikos, G. K., Athanasiadou, Maria & Triantaphylli, E. Die antibakterielle Wirkung des Tetracyclins, Oleandomycins und deren Kombination. Experimentelle Beobachtungen *in vitro*. [**Antibacterial Action of Tetracycline and Oleandomycin, alone or in Combination: *in vitro* Experiments**] *Deut. med. Woch.* 1960, May 27, v. 85, No. 22, 969–73, 992, 2 figs. [24 refs.]

The English summary appended to the paper is as follows:—

"The antibacterial effect of tetracycline and/or oleandomycin was tested in vitro on 253 bacterial strains, by means of serial dilution on solid agar nutrient medium. The sensitivity of the various strains was measured in dilutions of the antibiotic(s) from 0·3 to 20 μg./ml. When used in combination, the two antibiotics were mixed in the clinically usual proportion of 2 parts of tetracycline to one of oleandomycin. Of the 154 tested Staph. aureus strains, 102 were sensitive to both antibiotics, another 36 were sensitive only to oleandomycin, 5 only to tetracycline, while 11 were resistant to either. 59 strains of other bacteria were sensitive only to tetracycline, while 56 strains were resistant to either. Of 16 staphylococcus strains resistant to oleandomycin, 5 were sensitive to tetracycline. True synergism of the two antibiotics could not be shown. An additive effect was noted against 110 of the 253 strains. But this additive effect was not significant, since it was within the margin of error of the method. Similarly lacking in significance was the antagonism noted for 87 strains. The two antibiotics in combination were never more effective than would be expected from the amount of each in the pr paration. These results are compared with thos reported by others."

Hirsch, H. A. & Finland, M., with the technical assi tance of Clare Wilcox & Joan Yarrows. **Ant biotic Combinations: Antibacterial Action Serum after Ingestion of Novobiocin or Tetra cycline or Both.** *New England J. of Med.* 196 Feb. 4, v. 262, No. 5, 209–14, 2 figs. [10 refs.]

This is another of a series of iconoclastic papers b Finland and his colleagues on antibiotic combination The combination of tetracycline and novobiocin ha been reported by other workers to have a synergic actio particularly against staphylococci, not only *in vitro* b even *in vivo*. These authors gave a single 750 mgr dose of these antibiotics singly and mixed in 2 propo tions (2:1 and 1:2) to 8 normal men, and after 2, 4, 12 and 24 hours determined the minimum inhibitory co centration of their serum for 4 organisms, a streptococc and a staphylococcus sensitive to both antibiotics, and staphylococci each resistant to one of them. *In vitr* tests with the same mixtures showed no synergism, an the serum assays yielded results to be expected on simple additive basis, with one exception illustrating n synergism but antagonism or interference. When th assay organism was the tetracycline-resistant staph lococcus, 250 mgm. novobiocin produced slightly mo antibacterial activity in the serum when given alone tha when given with 500 mgm. tetracycline. *L. P. Garrod*

Blough, H. A., Hall, W. H. & Hong, L. **Seru Levels and Clinical Results with Erythromyci Propionate.** *Amer. J. Med. Sci.* 1960, May, 239, No. 5, 539–47. [13 refs.]

These authors from the University of Minnesota Med cal School gave equal doses of erythromycin in 3 form (base, stearate and propionate) and of triacetyl olea domycin to 10 normal subjects (laboratory personne and assayed the antibiotic in the blood 2 and 4 hou after a single dose (125 or 250 mgm.) and after the la of four 500 mgm. doses given at 8-hour interval Several assay methods were used. They confirmed th propionate is the best absorbed form of erythromyci giving blood levels about twice as high as the same do of the base in enteric-coated tablets. In terms of ant bacterial activity these levels are also higher than tho given by triacetyl oleandomycin. Apart from som observations confirming that each of these antibiotics more active in an alkaline medium than an acid, the re of the paper deals with clinical use. 50 patients, 26 whom had pneumonia and the remainder mostly infe tions of the throat, wounds or skin, the majority bei shown to be due to streptococci, pneumococci or staph lococci, were treated with erythromycin propionate wi generally gratifying results, sometimes after penicill had failed. A few brief illustrative case histories a given. 6 patients had side effects, 2 having diarrho and 1 each, nausea, pruritus and eosinophilia, a

"staphylococcal enterocolitis and pancreatitis" [the evidence supporting these last 2 diagnoses is not wholly convincing: the patient recovered from both conditions]. *L. P. Garrod*

HIRSCH, H. A., MCCARTHY, C. G. & FINLAND, M., with the technical assistance of Clare WILCOX & Joan H. YARROWS. **Polymyxin B and Colistin: Activity, Resistance and Cross-resistance** *in vitro*. *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 338–42.

Colistin (Colimycin) is known to resemble polymyxin B very closely, but according to these authors there are known chemical differences between them, including the presence in polymyxin B of d-phenylalanine. Their own work consisted of determining the minimum inhibitory concentrations of both antibiotics for multiple strains of 8 species of susceptible Gram-negative organisms. Polymyxin B was more active, with a difference of 2-fold or less, against intestinal Gram-negative organisms, and with differences of 3·4 and 4·0 respectively against gonococci and *Haemophilus influenzae*. There was complete cross-resistance when organisms were habituated to either, whether by repeated transfer on slowly rising concentrations (*Klebsiella aerogenes* and *Pseudomonas pyocyanea*) or in single step resistant mutants (*Kl. aerogenes* only) obtained in another way. *L. P. Garrod*

BROCK, T. D. & BROCK, M. Louise. **Effect of Novobiocin on Permeability of** *Escherichia coli*. *Arch. Biochemistry*. 1959, Nov., v. 85, No. 1, 176–85, 3 figs. [17 refs.]

These authors have shown by very ingenious methods that novobiocin in a concentration of 1 mgm./ml. acting on growing but not on stationary cells of *Escherichia coli*, produces an abnormal permeability, causing leakage of ribonucleic acid and permitting an enzyme to enter the cell from without. They suggest that the antibiotic may interfere with the synthesis of membrane material. [Bacterial species classifiable as sensitive to novobiocin are inhibited by a very small fraction of the enormous concentration used in these experiments. It seems at least possible, if not indeed likely, that they are attacked in a different way.] *L. P. Garrod*

BOYD, E. M. & PRICE-JONES, M. A. **The Comparative Acute Oral Toxicity of Spiramycin Adipate in Mice, Rats, Guinea Pigs, and Rabbits.** *Antibiotics & Chemotherapy*. New York. 1960, May, v. 10, No. 5, 273–84, 4 figs. [22 refs.]

GANGAROSA, E. J., JOHNSON, Thelma R. & RAMOS, H. S. **Ristocetin-Induced Thrombocytopenia: Site and Mechanism of Action.** *Arch. Intern. Med.* 1960, Jan., v. 105, No. 1, 83–9, 8 figs. [20 refs.]

Very large doses of ristocetin given intravenously to rabbits caused severe falls in the blood platelet counts, but without apparently damaging the marrow. Added to human blood *in vitro*, ristocetin in a concentration of 310 μgm./ml. or more [according to the text: 200 μgm./ml. is given as the limit in the legend of Fig. 6] also caused many of the platelets to disappear: some other antibiotics did not. Two case histories are given of patients in whom ristocetin caused thrombocytopenia. The authors believe that this antibiotic only destroys circulating platelets without affecting their formation, and suggest that this effect can be avoided by limiting the dose to 50 mgm./kgm. per day, and by not allowing the solution injected to exceed 1 mgm./ml. in concentration. [The strengths of the solutions with which these 2 patients were treated are not mentioned.] *L. P. Garrod*

NAGY, E., ALFÖLDI, L. & IVÁNOVICS, G. **Megacins.** *Acta Microbiologica*. Budapest. 1959, v. 6, No. 4, 327–36. [12 refs.]

Most of the studies of megacin by Iványovics and his colleagues have been carried out with that derived from a single strain of *Bacillus megaterium*, No. 216 [this *Bulletin*, 1960, v. 35, 282]. This paper inquires into whether megacins produced by other strains differ from it: 11 others were prepared and examined. None equalled that from 216 in antibacterial activity, but the degree of this activity and of capacity to destroy protoplasts corresponded closely in all megacins examined, indicating qualitative similarity. Antibacterial spectra were the same, except that *Bacillus anthracis* was resistant to megacin 216 (18/19 strains) but sensitive to some others: megacin 216 was also less active than others against *Micrococcus aurantiacus*. The main difference was revealed serologically: an anti-megacin serum prepared by immunizing rabbits with megacin 216 neutralized this megacin only: others were not only unaffected, but were themselves apparently non-antigenic. *L. P. Garrod*

GOLDBLATT, S. **Severe Reaction to Griseofulvin.** *J. Amer. Med. Ass.* 1960, Apr. 9, v. 172, No. 15, 1643–4.

A man aged 30 years, under treatment for hypertrophic lichen planus, observed "a flat, red circinate, scaly eruption on the anterior chest wall." This contained *Trichophyton rubrum*.

Subsequently, despite topical therapy, this lesion continued to spread to other parts of the body. There was also involvement of the toe-nails. Accordingly, oral griseofulvin was instituted, the patient receiving an initial course of 500 mgm. 4 times a day for 7 days and then 250 mgm. 5 times a day for another 7 days.

Response was manifested early to treatment in so far as itching ceased and regression of the lesions set in. However, 3 weeks later, the lesions began to spread again. 3 months later therapy with orally administered griseofulvin was resumed at a dosage of 250 mgm. 4 times daily. An eruption thereupon developed which, on further dosage, later spread rapidly and increased in severity. On examination, the patient presented with "an extensive swelling of the orbital, zygomatous, ear, and lip areas; figured urticarial lesions over the entire trunk

and extremities, with edema of the hands, wrists, feet, and ankles; and pain in the joints sufficient to produce almost complete limitation of motion." Treatment was instituted for this allergic reaction and the patient recovered; but shortly afterwards fungous lesions reappeared on the chest wall.

Investigation of this case continues.

C. J. La Touche

KOVÁCS, K., KÓTAI, A. & SZABÓ, I. **Synthetic Polypeptide Derivatives with Anti-Bacterial Activities.** [Correspondence.] *Nature.* 1960, Jan. 23, v. 185, 266–7.

These authors from Budapest first refer briefly to previous work on synthetic antibacterial polypeptides. These have the disadvantage that they are broken down by proteolytic enzymes in the body, but polymethyl-α-poly-L-glutamate when treated with ethylenediamine becomes stable. This substance, manufactured under the name Polyanthin, in a concentration of 3 mgm./ml. almost sterilized a suspension of tubercle bacilli in 5 days, and a single subcutaneous dose of 60 mgm. given to guineapigs 1 day after inoculation with tubercle bacilli retarded the development of this disease as compared with untreated controls at autopsy 93 days later.

L. P. Garrod

ADAMS, A., FREEMAN, W. A., HOLLAND, A., HOSSACK, D., INGLIS, J., PARKINSON, J., READING, H. W., RIVETT, K., SLACK, R., SUTHERLAND, R. & WIEN, R. **Sulphasomizole (5-*p*-Aminobenzenesulphonamido-3-Methyl*iso*thiazole): a New Antibacterial Sulphonamide.** *Nature.* 1960, Apr. 16, v. 186, 221–2. [11 refs.]

This paper from the Research Laboratories of May and Baker Ltd. describes the synthesis and some of the properties of a new sulphonamide, for which the name sulphasomizole has been officially approved. The *iso*-thiazole nucleus which it contains is said to have been hitherto unknown. Particulars are given of its solubility, antibacterial activity, action in experimental infections (each of these in general terms only), absorption and distribution in animals and man (including a few data on concentrations in cerebrospinal fluid) and tests of toxicity. Although the acetyl derivative has a low solubility and acetylation occurs, crystalluria has not been seen. Excretion is slow and therapeutic concentrations are maintained in the blood when only 2 daily doses are given. The sodium salt forms an almost neutral solution which can therefore be given intramuscularly [this appears to be the most distinctive property of this drug].

L. P. Garrod

MORRIS, E. J. & DARLOW, H. M. **Some Observations on Bactericidal Paint Films.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 64–72.

Germicides were added to paints, which were applied to sheets of cardboard and dried. These were placed in an exposure chamber into which various bacteria suspended in a buffer solution containing glycerin we sprayed and allowed to deposit on the painted surface They were then washed off: the germicide was neutr lized with a preparation containing egg yolk and Twe 20, and quantitative cultures were made. Results a expressed as percentage recoveries of bacteria in relatio to those recovered from a surface of paint containing r germicide.

All organisms used in the main experiments (*Strept coccus faecalis, Chromobacterium prodigiosum, Klebs ella aerogenes* and *Staphylococcus aureus*) were suscep tible to a roughly equal degree to most of the germicid used. The germicides used are classified in 2 groups quaternaries and other surface-active compounds, amon which Cetavlon (Cetrimide) was the most active, recoveries being 1·0 or less. Several of these compound greatly exceeded in activity any member of the other an miscellaneous group, which included phenols, phenyl me curic acetate, tetramethylthiuram disulphide, hexachlor phene, chlorhexidine, tri-*n*-butylin oxide and other salt and a proprietary self-sterilizing paint. Most of th tests were done in an atmosphere with a relative humi ity of 70%: when this was reduced to 40% germicida action was much reduced, particularly when blood o saliva was added to the bacterial suspension mediun Several types of paint were tried: those yielding a ver hard surface, such as epoxide resins, acquired litt germicidal activity.

Even the most germicidally active surface, that of urea-formaldehyde:alkyd resin containing Cetrimid lost most of its activity after 4 washings in water.

L. P. Garrod

WOODWARD, Marie F. & CLARK, Alice B. **Hospita Decontamination with Beta-Propiolactone Vapo** *U.S. Armed Forces Med. J.* 1960, Apr., v. 11, No 4, 459–63.

β-Propiolactone was sprayed with a power atomize in a sealed room containing various objects of furnitur clothing and medical equipment to give a concentratio of 100 mgm. per cu. ft. of air. The room was opene and ventilated after 2 hours; cultures made from its co tents were all sterile. After a further successful test i another room, the entire hospital (cubic capacity 89,00 cu. ft.) was treated in the same way, a sprayer mounte on a push-cart being taken round the building by a operator wearing protective clothing. On this occasio a *Bacillus subtilis* spore suspension was smeared on 3 sites, and 30 of these subsequently yielded no growt Both temperature and humidity were high when th experiments were done. No damage was caused, excep some blistering of varnished surfaces, attributed to co tact with the actual liquid. *L. P. Garrod*

GILLISEN, G. Die Abtötung von Tuberkelbazillen durc Beta-Propiolacton. [**The Killing of Tuberc Bacilli by Beta-Propiolactone**] *Desinfektion Gesundheitswesen.* 1960, Jan., v. 52, No. 1, 8–1 [26 refs.]

Dilutions of a 30% solution of β-propiolactone up t and including 1 in 200 regularly sterilized a 0·1 mgm

per ml. suspension of *Mycobacterium tuberculosis* H37Rv in 1 hour, both in water and in 10% serum. The same concentration killed tubercle bacilli in sputum dried on pieces of fabric, but a 1 in 1,000 dilution did not.

L. P. Garrod

DAWSON, F. W., JANSSEN, R. J. & HOFFMAN, R. K. **Virucidal Activity of β-Propiolactone Vapor. II. Effect on the Etiological Agents of Smallpox, Yellow Fever, Psittacosis, and Q Fever.** *Applied Microbiol.* Baltimore. 1960, Jan., v. 8, No. 1, 39–41.

Although β-propiolactone is known to be an efficient bactericide, its action on viruses has only been demonstrated for that of Venezuelan equine encephalomyelitis [this *Bulletin*, 1960, v. 35, 175]. Pieces of cotton fabric or paper were sprayed with virus suspensions and then exposed to β-propiolactone vapour generated with the same atomizer: exposure was for 15 minutes at 25°C. in an atmosphere of 90% relative humidity. The fabric or paper was then extracted and living virus was tested for quantitatively by the inoculation of chick embryos (smallpox and psittacosis viruses) mice (yellow fever) or guineapigs (*Rickettsia burneti*). All 4 were totally inactivated by a β-propiolactone concentration of 1 mgm. per litre of air. *L. P. Garrod*

VESELOV, M. P., KRUPENINA, A. A. & BLINOVA, L. A. **Investigations of the Bactericidal and Sporocidal Properties of Dichlorohydantoin and its Derivatives.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 4, 112–17. [Translated from Russian.]

The tests described here were made by immersing pieces of inoculated fabric in solutions of the disinfectant, treatment with a neutralizer (nature unspecified) and cultivation in broth. Dichlorohydantoin in aqueous solution killed *Staphylococcus aureus* and *Escherichia coli* in concentrations of the order of 0·01% in 1 minute, and in a concentration of 0·5–2% usually also killed spores of *Bacillus anthracis* in 1 minute, but in some tests there were survivors up to 1 hour. This substance was much less regularly effective when dissolved in acetone, ethanol or ethylene glycol (lesser activity in organic solvents being the general rule for disinfectants, the devotion of more space to these experiments than to those with aqueous solutions seems disproportionate). Dimethyldichlorohydantoin had a similar but somewhat lesser activity: diphenyldichlorohydantoin killed the vegetative bacteria only and not spores. *L. P. Garrod*

MOSES, P., MAGER, J. & FRANKEL, M. **Antimetabolic Activity of Amino Alkyl Sulphonic Acids and their Derivatives.** *Bull. Res. Counc. of Israel.* 1960, Apr., v. 9A, Nos. 1/2, 46–8, 1 fig.

"A number of α-amino alkylsulphonic acids and their peptide-like derivatives were found to cause a transient growth inhibition of *Escherichia coli* or *Proteus vulgaris*. The spontaneous reversal of the inhibition occurring at the end of the prolonged lag phase, appears to be due to the slow elaboration of metabolites, presumably amino acids accumulating in the culture medium. The growth retardation induced by the sulphonic acid analogues is nullified by the addition of an amino acid mixture to the growth medium. An hypothesis involving a feedback inhibition type of mechanism is advanced."

KLINE, Louise B. & HULL, R. N. **The Virucidal Properties of Peracetic Acid.** *Amer. J. Clin. Path.* 1960, Jan., v. 33, No. 1, 30–33.

Various disinfectants were added to tissue culture fluids containing poliomyelitis virus: after periods varying from 5 minutes to 24 hours the disinfectant was eliminated by chemical neutralization or dialysis and tissue cultures were inoculated with dilutions of the material to determine the degree of virus inactivation. This was complete in 5 minutes by 0·4% peracetic acid, which proved to be much the most active agent tested: an equivalent or lesser effect in a longer time was produced by such concentrations as 5% formaldehyde, 5% saponated cresol and 20% phenol. 4 other peroxyacids had similar but lesser activity. Peracetic acid was also active in low concentrations against some other viruses (ECHO, Coxsackie, adenoviruses, B virus and herpes simplex). It is recommended as a good decontaminating agent in virus laboratories, its only drawback being that its strong oxidation capacity damages metals and rubber.

L. P. Garrod

SAVAGE, R. H. M.; WILKINSON, G. R.; KELSEY, J. C.; BOWIE, J. H. **The Operation of Sterilising Autoclaves. A Symposium held at Brighton Technical College, School of Pharmacy, on May 9, 1959.** 45 pp., 18 figs. 1959. London: The Pharmaceutical Press, 17, Bloomsbury Square, W.C.1. [7s. 6d.]

There is much current interest in hospital sterilization techniques—a fact reflected by the number of conferences on this topic held in Britain in recent years. The four contributors to this symposium discussed various aspects of pressure-steam sterilization. Most of the information collected together here has been published elsewhere but the fact that it is gathered together in one place makes the symposium of value.

In the first paper (*Principles Underlying Steam Sterilisation* pp. 1–11) R. H. M. SAVAGE discusses the ways in which superheating of steam (in the broadest sense of the term) may arise in sterilization processes [see also this *Bulletin*, 1955, v. 30, 426], the behaviour of air-steam mixtures and the bacteriological reasons for preferring saturated to superheated steam for sterilization processes. On pp. 11–22, G. R. WILKINSON considers *The Design of Pressure Steam Sterilisers*. He deals with the physics of steam in relation to sterilizer design and then discusses the individual features of a sterilizer—the steam trap and by-pass [see also BARSON *et al.*, this *Bulletin*, 1959, v. 34, 373], vacuum pump, instrumentation and automatic control. Wilkinson explains the rapid penetration of steam into a load of dressings following a high pre-vacuum on

the basis that such penetration takes place before the pressure is high enough for condensation of the steam to take place. [In the description of a modern automatically controlled sterilizer the provision of different sterilizing cycles for dressings and rubber gloves is noted. This is a common feature of modern sterilizers which does not appear to have been justified. The provision of a time and temperature integrator covering the range 250–275°F. is mentioned but it is open to question whether an integrator should be expected to cover the whole of this range and thus attempt to compensate for gross and undesirable variations in steam supply.]

The third paper is by J. C. KELSEY on *Methods of Testing the Bactericidal Efficiency of Steam Sterilisers* (pp. 22–28). He points out the difficulties associated with testing sterilizers and describes the relationship between the thermal death times of various bacterial spores and the characteristics of an ideal indicator of a satisfactory sterilization process [see this *Bulletin*, 1958, v. 33, 603] and the times suggested by Perkins for contact between spores and steam to ensure sterility together with those suggested by a Medical Research Council Working Party [this *Bulletin*, 1959, v. 34, 807]. The various types of test are reviewed. Those using thermophilic bacteria or thermocouples require considerable experience. Browne's tubes are useful for day-to-day purposes but a daily inspection of the temperature and pressure records of a sterilizer is the most important single check on sterilizer efficiency.

The last paper, by J. H. BOWIE, deals with the *Operation and Use of Sterilising Equipment and Staff Responsibilities* (pp. 28–41). The responsibility of hospital authorities to staff and patients is discussed as are the difficulties which they encounter in inadequate and overcrowded hospitals. Other topics mentioned are the hospital infection committee and its function, central sterile supply, and sterilizing equipment for use outside the central supply department. Finally he describes work with an experimental sterilizer for bottled fluids (based on an Amsco model) in which the bottles can be cooled rapidly after sterilization.

A report of the discussion following the papers is appended (pp. 41–45).

[Those in charge of sterilization processes will find this a useful handbook on the theory underlying steam sterilization. For those unfamiliar with pressure-steam sterilization the maximum benefit will be derived if this book is read in conjunction with the report of the Medical Research Council's Working Party on Pressure Steam Sterilisers (*loc. cit.*).] *R. J. Fallon*

RUSSELL, F. & ABDURAHMAN, R. **Sterilization of Syringes by an Infra-Red Conveyor Oven.** *Scottish Med. J.* Glasgow. 1960, May, v. 5, No. 5, 213–18, 2 figs.

DARMADY *et al.* [this *Bulletin*, 1958, v. 33, 262] described an infra-red conveyor oven for sterilizing syringes. This paper reports tests made on such an oven supplied by Metropolitan Vickers Ltd. Balco crystal syringes were used in aluminium containers. Those for 2 ml. syringes were dulled inside and outside by boili in a caustic solution. Those for 10 and 20 ml. we dulled outside and painted matt black. The containe were sealed with Alka caps.

Tests with thermocouples confirmed the recommende initial "heating up" time of 1 hour. Bacteriologic tests with dust containing aerobic and anaerobic spor were satisfactory after a heating up time of 30 minut or longer. Browne's tubes, No. IV (12 minutes 180°C.) were changed from red to green after a heati up time of 45 minutes or more. In all cases the passag time through the oven was approximately 28 minute No ill effects were observed on the syringes after repeate sterilization. Thus the results of Darmady *et al.* we repeated and confirmed.

A new point is raised in this paper—the possibility re-contamination of the syringes by the aspiration unsterile air during cooling. It was deduced from th fact that the comparatively fragile metal cap remaine intact throughout the sterilizing process, and could not b airtight. Calculations based on Charles's Law and co firmed experimentally showed that a 20 ml. syringe co tainer could aspirate about 70 ml. of unsterile air c cooling from working temperature. Since the slit samp count of the ambient air was about 6 colonies per cu. f it was calculated that in these circumstances about 1 per 1000 20 ml. containers might be contaminated wi a single organism. Tests were made in which swab sterilized in capped metal containers were cultured. out of 30 were positive when cultured immediately aft cooling and 5 of 30 when cultured after overnight sto age. When a simple asbestos wool filter was fitted ov the cap 0 of 20 were positive. 3 out of 30 cultures sterile medium introduced asceptically into empty co tainers after sterilization were positive. In all cases th organism recovered was a micrococcus. It was thu concluded that a small but definite risk of re-contamina tion exists. Sterility tests made on 150 syringes ster lized under routine working conditions were only on positive, and then from a suspected faulty transfer.

It was decided to include a small absorbent cotto wool plug immediately inside the cap of each containe This would filter any aspirated air and also be availab as a swab for skin preparation. 15 syringes (20 ml.) protected were found to be sterile but 9 of the plu yielded an aerobic sporebearing organism. In anoth experiment 100 syringes (20 ml.) were found to be steri with 7 contaminated plugs.

An alternative precaution considered was to allow th containers to cool in a cabinet sterilized by ultra-viol light. All plugs cultured were sterile. In discussion it concluded that the technical difficulties of this metho limit its use.

The authors conclude the infra-red conveyor oven the most efficient economical and safe method for syring sterilization if the precautions they describe again re-contamination are taken. They also consider th Browne's tubes, No. IV, are the most useful routine te of satisfactory performance, that bacteriological tests sterilizing efficiency are unnecessary and that occasion sampling for re-contamination is of no value, because the low incidence expected. *J. C. Kelsey*

KAUFMANN, O. W., HARMON, L. G., PAILTHORP, O. C. & PFLUG, I. J. **Effect of Heat Treatment on the Growth of Surviving Cells.** *J. Bacteriology.* 1959, Dec., v. 78, No. 6, 834–8, 4 figs.

In studies on the pasteurization of milk at higher temperatures than those usually employed it was observed that small numbers of surviving bacteria multiplied only after a long delay. The authors asked themselves whether this was simply due to damage by heat, or to the mere fact that very few cells survived: in this connexion they cite the classical work of PENFOLD [*J. Hyg.* 1914, v. 14, 215], who showed many years ago that lag is prolonged by reducing the size of the inoculum. A suspension of a heat-resistant *Micrococcus* was serially diluted in sterile milk, which was then heated to 76°C. for 17 seconds or to 82°C. for 5 seconds, and immediately cooled. It was then incubated and viable counts were made at intervals. The lag period in control unheated milk was about 12 hours [why this should have been is not discussed]; heating to 76° and 82°C. prolonged the lag to 22 and 39 hours respectively in one representative experiment. This prolongation was less when survivors numbered 20,000 per ml. than when they were 2000. It thus seems that the density of the surviving population has some effect.

L. P. Garrod

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

BLAIR, J. E. & CARR, Miriam. **The Techniques and Interpretation of Phage Typing of Staphylococci.** *J. Lab. & Clin. Med.* 1960, Apr., v. 55, No. 4, 650–62, 2 figs. [27 refs.]

In this paper the authors describe their technique for the phage typing of staphylococci, and give details of the methods of phage propagation and testing. Their methods are developments of those described previously [WILLIAMS and RIPPON, this *Bulletin*, 1953, v. 28, 140; 662; BLAIR and CARR, *Ibid.*, 1954, v. 29, 105] and cannot usefully be abstracted in detail. Propagation is carried out by the soft-agar layer method. There is a brief discussion of the interpretation of typing results.

R. E. O. Williams

MEYER, W. & RISCHE, H. Epidemiologische Betrachtungen zur Variabilität von *Staphylococcus aureus.* [**Epidemiologic Considerations concerning the Variability of** *Staphylococcus aureus*] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 2, 156–66, 2 figs. [18 refs.]

Of 310 strains of *Staphylococcus aureus* isolated from noses of infants in a maternity hospital, 28·4% proved untypable by phage; 46·4% belonged to phage group I and within group I, 35·5% of all strains belonged to the type 52/52A/79/80. All of 17 type-80 strains were resistant to pencillin and streptomycin, but only 66 of 110 type-52/52A/79/80 strains. A further subdivision of the latter type was possible by means of the egg-yolk reaction and by testing with 2 supplementary phages known as 812 and 825.

40% of the strains from the infants' noses were resistant to penicillin and streptomycin, compared with 87% of strains from maternal mastitis. It is considered important to try to recognize and concentrate on preventing the spread of the more virulent types of staphylococci.

R. E. O. Williams

OEDING, P. **Staphylococcal Antigen-Antibody Reactions in Agar.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 1, 53–64, 6 figs. [21 refs.]

The toxin-antitoxin reactions of *Staphylococcus aureus* strain Wood 46 and its antitoxin were studied by the double diffusion technique in agar. 5 lines were obtained with concentrations of 20 u./ml. antitoxin and toxin 1:1. Lines 1–3 were weak and disappeared on dilution of the toxin. Lines 4 and 5 were strong and close together. A 6th line was present when antitoxin containing over 175 u./ml. was used. By suitable adjustment of toxin-antitoxin concentration 9 lines were obtained, lines 4 and 5 being complex.

Studies with different strains of coagulase-positive staphylococci suggested that part of complex 4, but not complex 5, was associated with haemolytic activity. Further studies showed that complex 4 was partially destroyed by heat while complex 5 was resistant to 60°C. Various components of complex 4 and 5 could be separated by precipitation with ethanol or ammonium sulphate and a single weak line of complex 4 nearest to the antitoxin cup was found to be associated with the α-haemolysin. The identity of the other lines was not established but they were not associated with β or δ haemolysin, coagulase or enterotoxin.

Rabbits were immunized with a vaccine prepared from 24-hour agar slope cultures of Wood 46 and the serum, when tested against Wood 46 toxin, produced no lines against complex 4 or 5, suggesting that these lines were due to toxins not present in the vaccine.

Active growth of strains on precipitation plates produced lines similar to those produced by the toxin-antitoxin system. Heat-killed organisms produced no lines when tested against antitoxin but strong lines against antibacterial sera. First washings of staphylococci grown on solid agar haemolysed rabbits erythrocytes and produced lines corresponding to complexes 4 and 5.

M. Patricia Jevons

JESSEN, O., FABER, V., ROSENDAL, K. & ERIKSEN, K. R. **Some Properties of *Staphylococcus aureus*, possibly related to Pathogenicity. Part I. A Study of 446 Strains from Different Types of Human Infection.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 3, 316–26, 2 figs. **Part 2. *In vitro* Properties and Origin of the Infecting Strains correlated to Mortality in 190 Patients with *Staphylococcus aureus* Bacteremia.** *Ibid.*, 327–35. [30 refs.]

1. A collection of strains of *Staphylococcus aureus* from various sources was examined for phage type and a number of physiological activities. Two thirds of the impetigo strains were in phage group II; types 80 and 52/52A/80 were the commonest (66%) in furunculosis and in bacteriaemia (41%). Nasal strains were distributed over the 3 groups. 81% of the bacteriaemia strains and 65% of those from furunculosis were penicillin-resistant. α-haemolysin production was not related to source except that nasal strains often produced small amounts. Impetigo staphylococci, especially the few in type 71, produced much hyaluronidase; type 80 produced only moderate amounts. A total of 923 strains were tested for the egg-yolk (EY) reaction; 87% were positive. Half the impetigo strains were EY negative; this was due to the fact that all the type 71 strains from this source were negative. Splitting of Tween was found to run parallel with the EY reaction.

2. A detailed comparison was made between the characteristics of staphylococci isolated from fatal and non-fatal cases of bacteriaemia. Antibiotic resistant strains were associated with a higher mortality than sensitive strains, as were strains giving a negative EY reaction. The latter association was observed in each of the antibiotic sensitivity categories. The association was also found within some phage types though the number of cases is small. The mortality for bacteriaemia acquired in hospital was higher than for that acquired outside. No association was found between mortality and the hyaluronidase or α-lysin production of the staphylococci.

R. E. O. Williams

BROWN, J. **Some Properties of Staphylococci related to Pathogenicity.** *J. Path. & Bact.* 1960, Apr., v. 79, No. 2, 257–62. [16 refs.]

Coagulase-positive staphylococci from patients at the Royal Infirmary, Glasgow, were grown on sheep's blood agar plates incubated in an atmosphere of 30% CO_2 in which was a central cup containing commercial antitoxin prepared against strain Wood 46. The type of lysin produced was determined and the number of antigen-antibody lines formed on these plates was counted. The α-haemolysin content of supernatants from nutrient broth cultures was assessed quantitatively.

A total of 400 strains were examined from 4 sources: (A) Primary lesions occurring through healthy skin. (B) Post-operative wound infections. (C) Infected burns. (D) Urinary infections.

α-lysin was produced by 399 strains and in general the more α-lysin produced the more flocculation lines were formed and the more complex the haemolytic patter Strains in groups A, B, C, D produced on average 5·5 4·74, 4·22 and 2·8 flocculation lines per strain respe tively, and strains of Group D produced only about on eighth of the lysin produced by strains in Group A.

M. Patricia Jevons

VÁCZI, L., HADHÁZY, G. & KATONA, M. **The Relatio of Surface Properties and Antibiotic Resistanc in *Staphylococcus aureus*. II. Phagocytosis Antibiotic Sensitive and Resistant *Staphylococci aureus* Strains.** *Acta Microbiologica.* Budapes 1959, v. 6, No. 4, 297–305, 1 fig. [18 refs.]

The method of these experiments was to mix a leuc cyte suspension from a rat peritoneum with rat seru and a suspension of staphylococci, and after 15 minut at 37°C. to count the cocci in 500 leucocytes. The err is said to be ± 10%. Two kinds of staphylococ were used, respectively sensitive and resistant multiple antibiotics. The first conclusion the autho reach, on which all the rest of their argument depends, that antibiotic-resistant staphylococci are also more resi tant to phagocytosis. [In these experiments both type were compared with a stock strain named Duncan: ratin the phagocytic index of this as 1·0, that of a sensitiv strain was 0·56 and of 2 resistant ones 0·35 and 0·33. N attempt is made to explain the greater difference betwee the sensitive and stock cultures: could not age sinc isolation and perhaps loss of toxigenic capacity accoun for this, and if so, how might this factor affect th other results?]

A strain artificially made resistant to 200 μgm./m chloramphenicol (number of transfers to produce th not stated) became not less but more susceptible to phago cytosis. The remaining experiments consisted of treatin suspensions chemically to determine what effect this ha on their susceptibility to phagocytosis. This was increase by potassium periodate in both sensitive and resistan strains, by sodium dodecyl benzenesulphonate in resi tant strains only, and by trypsin or cetyl pyridiniun bromide in neither. Resistant cells treated with lipas became resistant to the effect of sodium dodecyl ben zenesulphonate. A somewhat speculative argument base on these findings ends in the conclusion that antibioti resistance is accompanied by changes in the surface lipid of the bacterial cell.

L. P. Garrod

PETERSDORF, R. G., ROSE, Mary C., MINCHEW, H. B KEENE, W. R. & BENNETT, I. L., Jr. **The Sensitivit of Hemolytic Staphylococci to a Series of Anti biotics. II. A Three-Year Progress Report** *Arch. Intern. Med.* 1960, Mar., v. 105, No. 3, 398 412, 12 figs. [21 refs.]

This is a continuation of a previous study by th group of authors [this *Bulletin*, 1958, v. 33, 987] emplo ing similar methods. The 300 strains of staphylococ tested were isolated between July 1958 and April 1959 they consisted of 150 from patients with infections, 5 from the anterior nares of infected patients, and 10

"were contributed by patients and personnel without evidence of infection". All were haemolytic and formed black colonies on tellurite-glycine agar, but coagulase tests were not done. (It is admitted that some in the last group may have been non-pathogenic: 68% were non-phage-typable, as against 27% of those from infections, and their antibiotic sensitivities differed in some directions). Sensitivities to 13 antibiotics were determined by a tube dilution test (differences varying from 2- to 5-fold) with sub-culture to assess bactericidal action: the phage type of most was ascertained when possible, and some sensitivity tests were also done with discs.

The results are presented and analysed in a series of 30 graphs containing a great deal of interesting detail, although the separation of the strains into 3 groups, one of which probably includes some indifferent organisms, seems to complicate the findings unnecessarily. Some of the outstanding points are the high bactericidal activity of vancomycin (found more active than ristocetin) and kanamycin, none of which was included in the previous study; that resistance to chloramphenicol and erythromycin has not increased, and that Sigmamycin (more frequently called Signemycin) is no better than oleandomycin. These authors also express some personal views about how staphylococcal infections should be treated. They point out that 50% of strains are still sensitive to 50 units/ml. of penicillin [by the technique and with the size of inoculum that they use: it should be added that altering the latter could very much alter the result] and should therefore be controllable with very large doses, aided by chloramphenicol or erythromycin. For phage type 81 infections, this organism being highly penicillin-resistant, they suggest vancomycin and chloramphenicol, with substitutes for either according to the results of sensitivity tests. *L. P. Garrod*

RASKA, K., BEDNÁR, B., ROTTA, J., JELÍNEK, J. & MOTTL, J. **On the Question of the Virulence of Haemolytic Streptococci.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 4, 357–64, 10 figs. on 5 pls.

A number of experiments were made to compare the pathogenic effect of haemolytic streptococci of types 28 and 44, grown respectively in broth and in the rabbit's skin [following the method of SCHWAB *et al.*, this *Bulletin*, 1953, v. 28, 986], after intranasal inoculation into mice and rabbits. The streptococci grown *in vivo* tended to penetrate into the tissues much faster than those grown *in vitro*, and to give a higher death rate. [The experiments with mice were based on 1,500 animals but the reviewer found the diagram summarizing the results from them quite unintelligible.] *R. E. O. Williams*

CHESBRO, W. R. & EVANS, J. B. **Hydroxyl Ion Dependent Release of Amino Acids from Enterococci.** *J. Bacteriology.* 1960, May, v. 71, No. 3, 682–90, 8 figs. [20 refs.]

GALE, D. & LOCKHART, Elizabeth A. **A Rapid Mouse Test for the Diagnosis of Pulmonary Tuberculosis. III. Validation of the Test with Specimens from 1,000 Patients.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 715–25, 2 figs.

Previous communications [see this *Bulletin*, 1958, v. 33, 1174 *bis*] describe a mouse test for demonstrating within 20 days the presence of tubercle bacilli in pathological specimens. They now report their experiences with the method on 1,012 routine specimens from 362 patients.

The specimens were treated with 4% sodium hydroxide + 1% alum; 0·2 ml. of the centrifuged deposits, after neutralization, was injected intraperitoneally into 1 side of 4 mice, the other side having been inoculated immediately before with 0·8 ml. of 5% mucin. [The need for careful sterilization of this mucin at acid *p*H is stressed.] One mouse of each group was killed at 5, 10, 15 and 20 days, and impression smears and cultures were made from the organs (especially the spleen) which showed macroscopic evidence of tuberculosis.

The results are described in detail and from them the authors conclude that the method is not only more rapid, but it is also more sensitive than their usual cultural method. Of the 362 patients, 74 were positive by direct culture and the mouse test, 63 being positive by the latter test within 5 days, 64 were negative by direct culture and microscopy but positive by the mouse test, 33 being positive within 5 days, 5 were positive by the mouse test but the direct cultures were contaminated, and only 1 was positive by the direct culture (and this was positive on only 1 occasion) and negative by the mouse test.

Comparison of the results of the mouse smears with those of direct smears of the concentrates show that of the 911 specimens examined by both methods, 97 were positive by both tests, 78 by the mouse test but negative by direct smear, and only 1 was positive by direct smear but negative by the mouse test. Culturing the mouse organs was shown to be of little value, for of the 276 specimens positive by smear, 157 yielded either contaminated or negative cultures, there being only 1 that was positive by culture and negative by smear.

These experiences did not fully test the ability of the method to reveal atypical acid-fast bacilli as only 2 specimens yielded photochromogens and only 1 a scotochromogen; the organisms were, however, detected by the mouse method. *S. R. M. Bushby*

BERTE, S. J. & TUCKER, E. B. **The Comparative Specificity between Löwenstein-Jensen Medium and a Modified Oleic-Acid-Albumin Medium in supporting the Growth of Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1960, Apr., v. 81, No. 4, 595–7.

Specimens of sputum or gastric washings were treated with trisodium phosphate, and 0·5 ml. quantities of the deposits of each were inoculated on to 1 tube of Löwenstein-Jensen medium and 2 Petri dishes containing the modified oleic-acid-albumin medium. After incubation of the egg medium for 6 weeks and of the oleic acid medium for 4, tubercle bacilli were grown from 645 of the specimens, but whereas 41·2% of the specimens were

positive only on the egg medium only 5·3% were positive only on the oleic-acid medium.

The egg medium was thus obviously the better medium, and when the positivity of the specimens was related to the duration of the chemotherapy of the patients the superiority became even more apparent; of the positive specimens taken before or during the 1st month of chemotherapy, the incidence of positive culture on the oleic acid medium was 60% and this fell to approximately 44% with specimens from patients after 3 or more months of chemotherapy, whereas there was no decline in the incidence of positive culture on the egg medium as the duration of chemotherapy increased.

S. R. M. Bushby

FERTIG, S. Formy wzrostowe prątków na żółtku jaja kurzego. [**Growth Pattern of Tubercle Bacilli on the Yolk of Hen Egg**] *Archiwum Immunol. i. Terapii Dośw.* Warsaw. 1960, v. 8, No. 1, 77–100, 13 figs. [31 refs.]

The English summary appended to the paper is as follows:—

"The author used a new egg medium to investigate growth patterns of different varieties of acid fast tubercle bacilli. The medium was composed of a non-sterilized hen egg yolk diluted at the ratio of 1:5 with saline. In addition to yolk, the medium contained malachite green as a factor inhibiting the growth of other micro-organisms. The most luxuriant growth was observed to occur in the upper layers of a sediment which was formed in the medium some hours after it had been prepared.

"To observe the growth patterns of tubercle bacilli the microculture method was used with the medium yolk sediment acting as a supporting principle. The use of egg white as supporting principle yielded inferior results. The modified slide method (yolk used as a support) warrants the observation of unaffected growth patterns of tubercle bacilli in a comparatively short time (3–6 days). The investigation by this method comprised 19 tubercle bacilli strains including 2 human, 3 bovine, 2 avian, 6 BCG, 2 saprophytic types and 4 derived from diagnostic material. The experiments showed a great efficiency of the yolk as a medium for the investigation of the growth forms of human and bovine tubercle bacilli. Of 9 diagnostic strains used only one marked with No. 152 failed to show cord pattern which was consistent with the results obtained in the experiments on animals. Stock strains also exhibited in egg medium a far-reaching consistence of growth patterns with their virulence. Avian variants, namely slightly virulent D_4 and virulent 193 confirm the literature data pointing to the fact that the cord growth pattern is no constant feature of avian tubercle bacilli; saprophytic strains showed a considerable variability of their growth characteristics.

"The author demonstrated that the growth of highly virulent mammalian and avian tubercle bacilli strains on the egg medium used was quick and luxuriant. The results obtained corroborate the opinion of some investigators who claim that 'not all tubercle bacilli with cord growth are virulent but all virulent ones show cord pattern'. This suggests the possibility of using the given medium as a method of an early, approxima determination of the virulence of strains."

MEDVECZKY, E. **A Micromethod for the Routi Differentiation of Human Tubercle Bacilli fro other Mycobacteria in Primary Cultures.** *Am Rev. Respiratory Dis.* 1960, May, v. 81, No. 757–8.

The method depends upon the fact that human strai of tubercle bacilli produce much more nicotinic ac than do the bovine strains. 1 mgm. of tubercle baci from a Löwenstein-Jensen slope is homogenized in 9– mgm. of a 3% alcoholic solution of reagent grade ben dine, the benzidine solution being delivered from a sta dard Pasteur pipette and the homogenization being do with a glass rod in a conical centrifuge tube. The su pension is then added to a similar volume of 10% br mine cyanide in water. The bacteria become pale pi and the benzidine crystals a violet-pink within 10 minut the speed of development and the intensity of the colo depending on the amount of nicotinic acid prese Controls, consisting of the reagents with no bacteria and bovine tubercle bacilli with the reagents, should be use

For liquid cultures, equal volumes of culture and r agents may be used. The solutions are stable for seve weeks at 4°C.

S. R. M. Bushby

EIDUS, L., DIENA, B. B. & GREENBERG, L. **The U of *p*-Nitro-α-Acetylamino-β-Hydroxy-Propioph none (NAP) in the Differentiation of Myc bacteria.** *Amer. Rev. Respiratory Dis.* 196 May, v. 81, No. 5, 759–60. [Refs. in footnotes.]

This substance is an intermediate in the synthesis chloramphenicol and it has been shown to be 4 tim more active than the end product against the tuberc bacillus [this *Bulletin*, 1960, v. 35, 182].

In a modified Sauton medium with an inoculum fro a 10–14 day Dubos culture of 0·15 ml. per 9 ml. medium, the minimum inhibitory concentration of NA after 14 days' incubation was 5–10 μgm./ml. for human and 12 bovine strains of tubercle bacilli, 80 more for 12 avian strains (1 strain was inhibited by μgm./ml.), 40 or more for 61 chromogenic mycobacte and 80 or more for 8 saprophytic mycobacteria.

As NAP is not used for the treatment of disease use for distinguishing human and bovine tubercle baci from the other mycobacteria is recommended.

S. R. M. Bushby

EDWARDS, Lydia B., PALMER, C. E., AFFRONTI, L. HOPWOOD, Louise & EDWARDS, Phyllis Q. **Ep demiologic Studies of Tuberculin Sensitivit II. Response to Experimental Infection wi Mycobacteria isolated from Human Source** *Amer. J. Hyg.* 1960, Mar., v. 71, No. 2, 218–4 12 figs. [20 refs.]

This study was designed to investigate the infecti and sensitizing properties of 12 different acid-fast org nisms: 10 mycobacteria isolated from human sourc *Nocardia madurae* and Danish BCG.

12 groups of guineapigs were inoculated intracutaneously with the organisms and tested at intervals thereafter with PPD and other antigens prepared from several different mycobacteria including human-type tubercle bacilli. There was a 13th control group. The total number of animals was 671. Details of the infecting strains are given.

Before infection all animals were tested intracutaneously with 0·001 mgm. of PPD-S and PPD-B (Battey) combined, and only those found to be non-reactors at 48 hours were inoculated. All animals were tested with 6 antigens at 4 and 8 weeks, *viz.* PPD-S, PPD-B, avian PPD and derivatives of other organisms.

Mortality during the early months of the study was no greater in the infected groups than in the controls. No gross evidence of tuberculosis was found at autopsy. Weekly weighing of the animals showed that none of the organisms inoculated caused serious disease. The presence of local lesions at 2 weeks, except in the animals inoculated with *N. madurae* and the controls, showed however that the atypical strains used are capable of infecting guineapigs. The infections remained benign during the 4½ months of the study.

It was found that PPD antigens elicited reactions in nearly all the animals infected with the organisms from which the antigen was prepared. The results were remarkably similar for the several groups tested with homologous antigens. There was often cross-sensitivity to heterologous antigens but the reactions were generally smaller than to the homologous antigen.

There was evidence that some organisms produce a type of sensitivity that may be elicited by a variety of mycobacterial antigens, while other organisms produce sensitivity elicited almost exclusively by the homologous and closely related antigens. Corresponding differences may occur among the various PPD antigens so that some detect the sensitivity caused by several different organisms and others are more specific.

"Conversions" and "reversions" were found to be much less frequent for specific than for cross-reactions. Less than 10% of the animals tested on successive occasions with homologous antigen showed change from "positive" to "negative" or the reverse. More than half of the animals tested with heterologous antigens showed these changes.

It is inferred from the above experiments that in regions where the populations contain persons infected by different types of mycobacteria, a reaction to a particular antigen does not necessarily mean infection by the organism from which the antigen was prepared. It may, however, be possible to separate specific and cross-reactions by measurement since specific reactions are usually larger than the others provided the tests are done with PPD antigens corresponding to each of the different strains of organisms which infect and sensitize the individuals in the population. [See also this *Bulletin*, 1959, v. 34, 208.]

H. G. Calwell

SMITH, D. W., RANDALL, H. M., MACLENNAN, A. P. & LEDERER, E. **Mycosides: a New Class of Type-Specific Glycolipids of** *Mycobacteria.* [Correspondence.] *Nature.* 1960, June 11, v. 186, 887–8.

ARMSTRONG, A. R. **Time-Concentration Relationships of Isoniazid with Tubercle Bacilli** *in vitro. Amer. Rev. Respiratory Dis.* 1960, Apr., v. 81, No. 4, 498–503.

By growing tubercle bacilli in a chamber in which the medium could be changed at selected intervals by removal through a Millipore membrane filter, complete or nearly complete bacteriostasis was attained when the bacilli were exposed to concentrations of 2 μgm. isoniazid per ml. for 2 hours each day for 6 consecutive days; partial bacteriostatic effects were also observed with 0·5 μgm./ml., but concentrations as high as 16 μgm./ml. for a daily exposure time of 4 hours were necessary to kill the bacilli.

These preliminary experiments form part of a study being made in an attempt to account for the fact that 95% of Eskimos rapidly inactivate isoniazid and yet tuberculous Eskimos respond well to treatment with the drug. The present experiments were made with only 3 strains of tubercle bacilli, but they are being extended to include more strains and to throw light on the time-concentration relationship over the whole 24-hour period.

S. R. M. Bushby

TSUKAMURA, M., NODA, Y. & YAMAMOTO, M. **Genetic Studies on the Isoniazid Resistance-System of** *Mycobacterium tuberculosis* **var.** *hominis. Japanese J. Microbiol.* 1959, Apr., v. 3, No. 2, 113–23. [17 refs.]

This is a study of the distribution of degrees of resistance to isoniazid in individual clones of a strain of *Mycobacterium tuberculosis*, about 100 colonies being examined in each experiment. This distribution was fairly constant in colonies from media containing from 0·1 up to 50 μgm./ml. of isoniazid, and it is considered therefore that a single gene is responsible for mutation to this degree of resistance. A double mutation involving this gene and a second gene is believed to determine resistance above this level and up to 400 μgm./ml.

L. P. Garrod

MARK, H. J. **The Pathogenicity for Guinea Pigs of Isoniazid-Resistant Tubercle Bacilli isolated from Patients on a High-Dose Isoniazid Regimen.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 752–6.

This paper is an attempt to relate isoniazid resistance, catalase activity and virulence for guineapigs with the clinical progress of the patient.

Tubercle bacilli from 20 patients undergoing treatment with 800 mgm. isoniazid and 100 mgm. pyridoxine each day were inoculated into pairs of guineapigs, a total of 51 pairs being used, and the animals were killed at various intervals. As the value of the results with the first 7 patients was reduced, because the pairs of guineapigs were killed on the same day so that any evidence of regression of the lesions could not be observed, the

killing of each animal of the pairs inoculated with the other strains was staggered.

From the results the author concluded that there is no clear-cut relationship between virulence and catalase activity, and that generalizations with respect to the problem of the virulence of these strains must be viewed circumspectly, each patient being approached on an individual basis. The variations in catalase activity shown by cultures of the tubercle bacilli isolated from 6 patients at monthly intervals emphasized even more the obvious problem of deciding whether a patient is still infected with pathogenic bacilli. *S. R. M. Bushby*

Caló, A. & Evdokimoff, Vera. Nuovi derivati della pirazinamide ad azione tubercolostatica. [**New Derivatives of Pyrazinamide with Tuberculostatic Action**] *Rendiconti Istituto Superiore di Sanità.* Rome. 1959, v. 22, Pts. 11/12, 1107–16. [10 refs.] English summary.

Steenken, W., Jr. & Montalbine, V. **The Antituberculous Activity of Thioamide *in vitro* and in the Experimental Animal (Mouse and Guinea Pig).** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 761–3.

Alpha-ethyl-thio*iso*nicotinamide (TH 1314) has been reported to be active against isoniazid-resistant tubercle bacilli [Rist *et al.*, this *Bulletin*, 1959, v. 34, 621] and in this study it has been shown to inhibit H37Rv at concentrations of 3·1 μgm./ml. in Dubos medium and at 0·4 μgm./ml. in Proskauer and Beck medium, but when 10% horse serum was added to the latter, 12·5 μgm./ml. was required; a pigmented unclassified strain of mycobacteria was inhibited by 12·5 μgm./ml. in Dubos medium. The drug was tuberculocidal at 25 μgm./ml. when tested after 18 days at 37°C. H37Rv became resistant to 200 μgm./ml. after 18 passages in drug-containing Dubos medium.

In guineapigs infected with 0·1 mgm. of H37Rv subcutaneously and treated for an unspecified period, TH 1314 at 10 mgm./kgm., afforded much less protection than 20 mgm. streptomycin per kgm. or 2·5 mgm. isoniazid per kgm., judged by the extent of the disease in the lungs, liver and lymph nodes. In mice infected intravenously with 0·1 mgm. of a TH 1314-resistant variant of H37Rv, 0·25 mgm. TH 1314 in the daily feed afforded no protection whereas 0·025 mgm. of isoniazid gave very high protection. *S. R. M. Bushby*

Steenken, W., Jr., Montalbine, V. & Smith, M. M. **Antituberculous Activity of Rimino Compound of the Phenazine Series.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 764–7.

This Rimino compound is B663 of the phenazine series [Barry *et al.*, this *Bulletin*, 1957, v. 32, 245, 945]. In the present study it was shown to inhibit H37Rv in Dubos medium and Proskauer and Beck medium at 0·31 μgm./ml., and in Proskauer and Beck medium + 10 horse serum slightly at 2·5 μgm./ml., and to inhibit isoniazid-resistant variant of H37Rv and a pigmented u classified strain of mycobacterium at about these sa concentrations. Against H37Rv the drug was tubercul cidal at 0·62 μgm./ml. when tested after 14 days at 37° and after 14 passages in medium containing sub-inhil tory concentrations of the drug, this strain did not lo its susceptibility. [In the summary the authors state th it did lose its susceptibility.] In guineapigs infected intr cardially with 0·1 mgm. of either H37Rv, a bovine stra of tuberle bacilli, or an isoniazid-resistant variant of t latter, B663 had, however, little effect on the course the disease. The doses used were 5 or 10 mgm./kg per day, whereas similar doses of isoniazid gave ve high protection against the isoniazid-susceptible strai

This poor protection by B663 is in contrast to the hi activity reported by Barry [*Ibid.*, 1957, v. 32, 945], b the present authors attribute the discrepancy to the d ferences in the routes of infection; the intracardial rou produces a widely disseminated infection against whi only highly active drugs such as isoniazid or strept mycin are effective. *S. R. M. Bushby*

Acharya, B. K., Robson, J. M. & Sullivan, F. M **Antituberculous Activity of a Phenazine Deriv tive (B663).** *Amer. Rev. Respiratory Dis.* 195 Dec., v. 80, No. 6, 871–5, 4 figs.

Rosenthal, S. R. & Williston, E. H. **Factors infl encing the Activity of BCG in the Process Freeze Drying.** *Acta Tuberculosea Scandinavic* 1960, v. 38, No. 2, 140–52, 1 fig. & 1 pl. [21 refs

In a comparison of the viability and antigenicity BCG suspended and freeze-dried in S/4 suspendi medium + 15% lactose, the freeze-dried vaccine h only 70% of the viability of fresh vaccine but its an genicity in guineapigs and infants was the same as th of the fresh vaccine. Stability tests, assessed by cordi properties, local skin reactions, intraperitoneal patholo in guineapigs, tuberculin conversion in animal and ma and resistance produced in mice, to an intravenous cha lenge with H37Rv, showed that the dried vaccine co pared favourably with the liquid vaccine.

Electron photomicrographs taken in an attempt explain the role of the adjuvants in freeze-drying, showe shrinkage of the cytoplasm of the bacilli suspended S/4 + 15% lactose, suggesting protection by dehydratio This explanation was supported by: (1) the fact th exposure to the lactose for 3 hours before freezing ga optimal viability to the vaccine, and (2) that the additio of 1·5% glycerol even further increased the viabilit An alternative explanation, however, is that the adjuvan protect certain enzymes, and estimation of the endoge ous respiration and of the catalase, nitrogen reducta and urease activities showed that freeze-drying has differential effect on enzymes; a preliminary experime in which nicotinic acid amide, the most common growt factor needed by bacteria, was added to the adjuva indicated that it improved the viability and antigenicit

of the vaccine. Further observations showed that the addition of 0·025% Triton to the additive lessens viability during storage.

The mechanism by which sodium glutamate acts as a protective adjuvant is also unknown but experiments show that the optimum concentration varies with the strength of the vaccine. The strength of the vaccine was also shown to alter both the optimum freezing temperature and the optimum time cycle of drying; −15° to −30°C. seems most suitable for 10 mgm./ml. vaccine and −45° to −70°C. for 50 mgm./ml. vaccine. Sealing the ampoules with dry nitrogen is apparently adequate for storage up to 5°C., but vacuum sealing is required for adequate storage at room or incubator temperature.

S. R. M. Bushby

TOLDERLUND, K., BUNCH-CHRISTENSEN, K. & WAALER, H. **Development and Duration of BCG-Induced Allergy in the Guinea-Pig.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 1/2, 177–84, 3 figs. [16 refs.]

There have been many investigations into the development and duration of BCG-induced allergy in the guineapig but as the animals were frequently tested with tuberculin the results were probably influenced by the boosting and desensitizing effects of the tuberculin [this *Bulletin*, 1958, v. 33, 334]. In the present studies, which consisted of 2 experiments with 270 and 394 guineapigs, respectively, the animals were vaccinated with 0·1 ml. doses of the standard strength vaccine (0·75 mgm./ml.) diluted 10^{0}, 10^{-1}, and 10^{-2}, and tested at intervals ranging from 1 to 13½ months, with 10 TU of PPD. For assessing the effects of the tuberculin on enhancing the allergy, half the animals were given an injection of 10 TU of tuberculin 2 weeks before the degree of allergy was assessed.

The results show that the sensitivity is apparent 1 week after vaccination, attains a maximum within 1–2 months, remains stable for 1 month, and then steadily decreases so that by 12 months the sensitivity has almost disappeared.

In the animals given the booster dose of tuberculin the maximum allergic response was not affected but it enhanced the allergy in the animals in which the allergic state was waning to such an extent that the maximum response still occurred 5 months after vaccination, and even when the booster dose was delayed for 13½ months it still induced sensitivity to the test dose.

The authors conclude that 6 weeks after vaccination is the best time for tuberculin testing of guineapigs used in the control of BCG. *S. R. M. Bushby*

TOLDERLUND, K., BUNCH-CHRISTENSEN, K. & WAALER, H. **Development and Course of Tuberculin Allergy in Guinea-Pigs Vaccinated with Various Doses of Danish Liquid BCG Vaccine.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 1/2, 185–96, 4 figs. [24 refs.]

This paper, which represents the first step in an examination into the problem of using the guineapig for assessing the biological activity of BCG, deals with the relationship between the degree of tuberculin sensitivity and the dose of BCG. The WHO Expert Committee on Biological Standardization laid down that 5 mgm. of BCG injected into the guineapig should produce a standard reaction to tuberculin but it is well known that a much smaller dose of BCG can produce allergy in this animal.

In 2 experiments, with 403 and 698 guineapigs respectively, a single dose ranging from 10^{0} to $10^{-8} \times 0{\cdot}075$ mgm. semi-dried culture of BCG was injected intradermally and from 1–42 weeks later the animals were tested with 2 and 20 TU of PPD; each animal was tested only once with the tuberculin thus eliminating the possibility of tuberculin affecting the allergic response.

The results show that although allergy is definitely produced by $10^{-5} \times 0{\cdot}075$ mgm. BCG, the speed of its development and its intensity are dependent on the size of the sensitizing dose, *e.g.* whereas the 0·075 mgm. dose caused the development of a maximum allergic response of 16 mm., after 5 weeks, the maximum was 14 mm. after 8 weeks with 10^{-2} of this dose, and 12 mm. after 15 weeks with 10^{-5} of this dose. Thus although with doses ranging from 0·075 mgm. to 10^{-4} of this dose, there was no difference in the reactions at 12 weeks, it would seem more promising if vaccines were assayed by the speed of the development of allergy. *S. R. M. Bushby*

PASQUIER, J. F. & ZAJDELA, F., with the technical assistance of H. CHALVET & Y. LUCEL. Étude de la vaccination de la souris par le vaccin BCG, au moyen des autoradiographies. [**Studies, by means of Autoradiography, on Immunization of Mice by BCG Vaccine**] *Ann. Inst. Pasteur.* 1960, Mar., v. 98, No. 3, 383–97, 16 figs. (6 coloured) on 4 pls. [20 refs.]

In the introduction to this paper the authors discuss the value of radio-active labelled bacilli in experimental tuberculosis and they then describe in detail an experiment in which mice were injected intravenously with ^{14}C-labelled virulent tubercle bacilli, half of the animals having been vaccinated with BCG 6 weeks earlier. Some of the mice were killed 48 hours after challenge and the others after 15 days. Stained sections and auto-radiographs of sections of the lungs and the spleens of the vaccinated and non-vaccinated animals were then compared.

Details are given of labelling the bacilli by growing them in a medium containing sodium acetate labelled with ^{14}C in the methyl group [this *Bulletin*, 1956, v. 31, 1259], and the technical details of the methods of preparing the auto-radiographs of the sections are outlined.

Comparison of the sections revealed little difference in the number or the distribution of the bacilli in the vaccinated and control mice, although the radio-active method revealed the presence of more bacilli than did the acid-fast staining method. In the sections of the animals killed 15 days after challenge, the number of bacilli in the unvaccinated mice had increased many times and there was definite evidence of tuberculous changes in the tissues. In the vaccinated animals, killed at this stage of

the infection, the increase in the number of bacilli was variable; in some animals it was very low and in others the sections were indistinguishable from those of the control animals. *S. R. M. Bushby*

WEISS, D. W. & WELLS, A. Q. **Vaccination against Tuberculosis with Nonliving Vaccines. II. Vaccination of Guinea Pigs with Phenol-Killed Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1960, Apr., v. 81, No. 4, 518–38. [33 refs.]

In previous papers [see this *Bulletin*, 1960, v. 35, 460], one of the authors showed that non-living vaccines afford high protection against the tubercle bacillus, and the purpose of the present paper was to report the results of vaccinating guineapigs with phenol-killed tubercle bacilli under a variety of conditions.

The vaccine consisted of human virulent tubercle bacilli, which had been suspended in 2% phenol for 24 hours, washed with water and cold acetone and then air-dried; it was used within 4 months of preparation and ground in a Teflon tissue grinder before being injected. The challenge organism was the Vallée strain of bovine tubercle bacilli and was administered either intramuscularly or by inhalation. The effects of the vaccination were assessed by the prolongation of the survival time.

In the 1st experiment graded doses (1·5–24 mgm.) of the vaccine were injected subcutaneously and intraperitoneally, some of the animals receiving the vaccine suspended in Freund's adjuvant. Other animals were vaccinated with BCG or with phenol-killed *Mycobacterium phlei*. Challenge was 6 weeks after vaccination.

In the 2nd experiment the administration of the vaccine (1·0 mgm.) was repeated weekly for 6 doses, or fortnightly for 3 doses, the vaccine being suspended either in saline or Freund's adjuvant. The challenge was made 12 weeks after the 1st dose of vaccine.

In the 3rd experiment, in which the vaccine was given in single and multiple doses, the challenge was delayed for 36 weeks.

The results of the experiments confirmed that non-living vaccines can be as effective as living vaccines, but their efficacy will vary under different conditions. With the phenol-killed vaccine the best protection was given with small doses, *e.g.* a single intraperitoneal injection of 1·5 mgm. in saline or 0·5 mgm. in the adjuvant afforded somewhat better protection than living BCG, and even when the challenge was delayed for 5 months the protection was of the same order as that given by the living vaccine. When suspended in the adjuvant the vaccine appeared to be more effective when given subcutaneously than when given intraperitoneally. There were no gross manifestations of toxicity and when there was any retardation in weight-gain or evidence of illness, it was only transient.

The development of hypersensitivity was assessed in a separate experiment and the vaccine was shown to cause reactions to tuberculin of the same order as those induced by BCG.

In the authors' opinion, these results offer once again every indication that killed vaccines should be given serious attention for use in man. *S. R. M. Bushby*

GERNEZ-RIEUX, C., TACQUET, A. & MACQUET, V. Étu du pouvoir pathogène pour l'animal des myc bactéries atypiques. Influence du virus grippal du quartz sur l'infection expérimentale. [**Path genicity for Animals of Atypical Mycobacteri Effect of Influenza Virus and of Quartz on E perimental Infections**] *Ann. Inst. Pasteur de Lil* 1958–1959, v. 10, 9–28, 2 figs. [20 refs.]

During the last 3 years 45,000 pathological specime were examined by the authors for mycobacteria, a from these 80 strains of atypical mycobacteria were is lated. 22 of these strains were photochromogens a they came from 8 patients, 6 of whom were coal-mine 22 were scotochromogens and these came from patients; 36 were non-photochromogens and these car from 10 patients, 4 of whom were miners. From only patient was the tubercle bacillus isolated as well as t atypical mycobacterium, and this strain was a non-phot chromogen. Comparison of the isolation recovery ra by either the 4% caustic soda method or the Teepol-1 caustic soda method, showed that the latter was t better, and the comparison also showed that 0·75% gl cerol in the medium increased the recovery rate of the bacilli. The photochromogens were found to be general less resistant to chemotherapeutic agents th were the other types.

None of these strains produced progressive disea when injected subcutaneously into guineapigs. Inject intradermally, the photochromogens produced mo intense local reactions at about the fifth day than did t other strains, and when injected intraperitoneally, t involvement of the liver and lungs was also more pr nounced with the photochromogens. Injected intrave ously into mice the photochromogens again proved t more virulent.

None of the strains produced progressive lesions in t rabbit and chicken, but when injected intraperitoneal into the hamster, the photochromogens produced tube cles in the lungs and an enlargement of the spleen a lymph nodes.

No increased virulence was observed when the myc bacteria and the influenza virus were inoculated togeth into guineapigs. Inoculation of the bacilli with a su pension of fine particle quartz (3μ) had little effect the lesions when the injection route was subcutaneous intraperitoneal but when it was by inhalation the pu monary lesions were definitely more severe.

S. R. M. Bushby

CALALB, G., SARAGEA, Alice, MAXIMESCU, Paul IEREMIA, T. & TAGA, Stefania. Studiu comparat asupra metodelor de cercetare a toxigenității tu pinilor de *C. diphtheriae*. [**A Comparative Stud on the Methods used for the Investigation of *diphtheriae* Strains**] *Microbiol., Parazitol., Ep demiol.* Bucharest. 1959, Sept.–Oct., v. 4, No. 429–37, 3 figs. [30 refs.] English summary.

A comparison of the toxigenicity of 175 strains *Corynebacterium diphtheriae* isolated from patients a carriers in 1957–58 in Rumania has been made by

ivo and *in vitro* tests. 99 strains were found to be oxigenic by the Fraser intradermal test in rabbits, 98 by el diffusion-precipitation, 96 by the intradermal and 93 y the subcutaneous test in guineapigs, and 16 by the Ramon flocculation test. Of the 99 toxigenic strains 46 vere of type *gravis*, 42 were *mitis* and 11 *intermedius*; 0 toxigenic strains were lysogenic and 28 were sensitive o 1 or several diphtheria phages. *D. J. Bauer*

GUNDERSEN, W. B. **Investigation on the Serological Relationships of *Corynebacterium diphtheriae*, Type *mitis*, and *Corynebacterium belfanti*.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 1, 65–74, 4 figs. [18 refs.]

The author has sought to determine how far the corynebacteria isolated from cases of ozaena and distinguished from the *mitis* variants of *C. diphtheriae* by their inability to reduce nitrate and lack of lethal toxin can be differentiated among themselves and from *mitis* strains by agglutination and by the production of lines of precipitation in gel diffusion plates.

These ozaena strains, for which the name *C. belfanti* has been accepted, are found to be split into 2 main groups, both distinct from all *mitis* strains tested by agglutination and absorption of agglutinins.

The results with gel diffusion methods were less clearly cut. A diffuse line near to the antigen basin was peculiar to the first group of *belfanti* strains and not found in the *mitis* strains. There were, however, a number of sharper lines of precipitation which were common to both *belfanti* groups and to many of the *mitis* strains.

The possibility is suggested that the gel diffusion method of observation may reveal relationships within the group of corynebacteria which are not revealed by agglutination. *J. W. McLeod*

RELYVELD, E. H., VAN TRIET, A. J. & RAYNAUD, M., with the technical collaboration of O. BEPOLDIN & W. J. VAN RHEE. Étude immunologique de sérums de moutons antidiphtériques. [**Immunological Studies of Antidiphtheritic Sera prepared from the Sheep**] *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 4, 369–402. 11 figs. [Numerous refs.]

The sheep were prepared with injections of both purified and crude formol toxoid, and crude and purified toxins were used in preparing the mixtures of toxin and antitoxin for constructing neutralization curves. Observations were also made on the electrophoretic mobility of the antibodies produced, and with iodine 131 a marked toxin was produced which facilitated observations on the distribution of toxin between supernatants and precipitate in the course of observing graded mixtures of toxin and antitoxin set up to establish the neutralization curves.

The chief outcome of these observations was to show that neutralizing antibody was produced more readily than flocculating antibody so that the ratio Lr/Lf for such sera is high. This peculiarity of the serum is associated with a large increase of globulin which in its electrophoretic mobility is intermediate between the beta 2 globulin and the gamma globulin of the horse. The letter S is suggested to distinguish such globulins. The neutralization curves produced are intermediate in type between the rabbit or precipitation form and the horse or flocculation type. It was calculated that at the outset of precipitation in graded toxin-antitoxin mixtures the formula for the complex was approximately TA 10, whereas at maximum of precipitation it was TA 4.

J. W. McLeod

LACEY, B. W. **Antigenic Modulation of *Bordetella pertussis*.** *J. Hygiene.* 1960, Mar., v. 58, No. 1, 57–93, 16 figs. [Numerous refs.]

The author demonstrated that the antigenic structure of *Bordetella* [*Haemophilus*] *pertussis* varies continuously with growth conditions. High temperatures and certain ions such as sodium, potassium, halides, formate and nitrate favoured the "X mode" of growth resembling that seen on Bordet and Gengou medium at 35°C. Low temperatures and other ions such as magnesium, sulphate and mono- or di-carboxylic acids with more than 2 carbon atoms favoured a different growth form, the so-called "C-mode" characterized by failure to agglutinate red blood cells, lack of haemolytic activity, failure to be agglutinated by salts of heavy metals and a changed surface antigenic structure. A third mode the "I mode" was induced within a narrow range of intermediate temperatures and ion ratios.

The change from one mode to another (modulation) occurred without mutation or selection and was complete within 7–15 cell divisions.

Antigens characteristic of the "X-mode" showed strain variation and reacted with antisera to *B. parapertussis* and *B. bronchiseptica* while cells in the "C-mode" had no surface antigens related to these organisms and were serotypically homogeneous.

Convalescent sera showed mainly antibodies for the "X-mode" but "C-mode" antibodies were found in several adults with persistent cough and infection. The author discussed the significance of modulation with regard to whooping cough and vaccine production.

John R. Norris

PRESTON, N. W. & TE PUNGA, W. A. **The Relation between Agglutinin Production by Pertussis Vaccines and their Immunising Potency in Mice.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 209–16. [18 refs].

"Rapid shaking techniques for agglutination and for agglutinin-absorption have been used. The complex nature of the surface antigenic structure of different strains of *Haemophilus (Bordetella) pertussis* has been confirmed. We have shown that these type-specific agglutinogens could account for the lack of correlation between agglutinin production and immunogenicity of pertussis vaccines observed by those who have ignored

such strain differences. It is suggested that one or more of the agglutinogens may be associated with immunity and that this association should be investigated in more detail. The possible relationships of these properties to haemagglutinin and to the histamine-sensitising factor (HSF) are discussed."

STUY, J. H. **Studies on the Radiation Inactivation of Microorganisms. VI. X-Ray-Induced Breakdown of Deoxyribonucleic Acid in *Haemophilus influenzae* and in Other Bacteria.** *J. Bacteriology.* 1960, May, v. 79, No. 5, 707–15, 10 figs. [14 refs.]

DAVIS, I., SELLERS, W., ORBACH, H. & WEDDINGTON, G. **An Evaluation of Several Media for the Early Detection of *Pseudomonas aeruginosa* encountered in Clinical Practice.** *J. Lab. & Clin. Med.* 1960, Jan., v. 55, No. 1, 139–43, 2 figs.

Approximately 100 strains of *Pseudomonas aeruginosa* [*pyocyanea*] were grown on 3 different culture media: nutrient agar, asparagine agar and Sabouraud maltose agar. The results were compared with regard to the production of the characteristic pigment and it was found that the Sabouraud maltose agar was significantly superior to the other media in that the chances of detecting pigmentation with this medium within 24 hours was greater, and there was an increased degree of pigmentation with the strains tested after incubation for this period. *H. J. Bensted*

TAMIMI, H. A. **The Effect of Buffered Glycerol Saline and Formalized Buffered Glycerol Saline on the Viability of Enteric Bacteria and Enteric Phage.** *J. Infect. Dis.* 1959, Nov.–Dec., v. 105, No. 3, 274–9. [16 refs.]

There is already a good deal of evidence to show the value of buffered glycerol saline in preserving *Shigella* and *Salmonella* organisms. Formolized buffered glycerol saline was introduced with the object of inactivating the *Shigella* bacteriophages since it had been suggested that the poor isolation rate of *Shigella* organisms from dysentery patients was due to the activity of the dysentery phages.

The present author has re-investigated the problem and extended its scope to include other members of the Enterobacteriaceae. The findings indicate that buffered glycerol saline inhibits the growth of all the intestinal Gram-negative bacteria studied but preserves a small number of the bacterial cells in a viable static state. It also inactivates bacteriophages that are present and enhances the isolation of the bacteria from selective media. Formolized buffered glycerol saline had no advantage over the simple buffered glycerol preparation in inactivating *Shigella* bacteriophages. *H. J. Bensted*

TIMAKOV, V. D. & GOLDFARB, D. M. Reakce vzestu titru baktériofága jako metoda diagnostiky infel nich onemocnění a zjuštování patogenních bakte **[The Phage Titre Increase Test as a Method diagnosing Infectious Diseases and detecti Pathogenic Bacteria]** *Ceskoslov. Epidemiol., M robiol., Imunol.* Prague. 1959, v. 8, No. 6, 361- [16 refs.] English summary.

The phage titre increase test has been widely used the Soviet Union for detecting the presence of pathoge organisms of the enteric group [this *Bulletin*, 1959, v. 68; 1960, v. 35, 77], and the method is reviewed in present paper. Phage specific for the organism to detected is added in a known dose to the material to investigated and the mixture is then incubated; pha particles which encounter the susceptible organisms w undergo a cycle of multiplication, causing a rise in t titre which is detected by plating dilutions on an in cator organism, and which is indicative of the presen of the specific organism in the sample examined. T method has the advantage of rapidity, since it is unnec sary to attempt to isolate and identify a pure cultu and is also considered to be more sensitive than conve tional bacteriological methods. The strain of phage s ected for use should be easily adsorbed, and should ha a short cycle time and a high yield. The method h been used to detect *Shigella flexneri, Sh. flexneri* v *newcastle, Sh. sonnei* and *Salmonella typhi*, and can applied to the investigation of stools, urine, milk a water. *D. J. Bauer*

BAKER, E. E.; WHITESIDE, Roberta E.; BASCH, DEROW, M. A. **The Vi Antigens of the Enter bacteriaceae. I. Purification and Chemical Pr perties** [BAKER, WHITESIDE, BASCH & DEROW *J. Immunology.* 1959, Dec., v. 83, No. 6, 680–8 2 figs. [33 refs.] **II. Immunologic and Biolog Properties** [WHITESIDE & BAKER]. *Ibid.*, 687–9 3 figs. [18 refs.]

I. The organisms used in this study were *Salmonel typhi* Ty2 and strain 61, *Escherichia coli* strain 136, a the ballerup [*Bethesda ballerupensis*] strain 481. The antigens were prepared by growing the organisms in completely dialyzable medium and then killing and dr ing them with acetone. The acetone-dried organisr were suspended in 0·15 M sodium chloride and aft standing for about 2 hours, the suspension was mix with 2 volumes of 95% alcohol and the bacilli togeth with dissolved O and Vi antigens were precipitated. Th material was collected by centrifugation and extract with 60% ethanol in 0·15 M NaCl at 37°C. for 18– hours. The extraction procedure was repeated sever times and a double diffusion agar precipitin meth was employed to follow the course of purification and establish the serological homogeneity of the purifi preparations. Many of the preparations still contain small amounts of O antigen in spite of the fact th electrophoretic analysis showed a single component.

II. The purified Vi antigens isolated from *Sal typhi*, strains Ty2 and 61, *E. coli* and ballerup we

xamined by the agar diffusion precipitin technique and ound to be identical serologically. Acetone-killed whole acilli were better immunizing agents than the purified ntigens isolated from them. In contrast to some other vorkers, the authors found that Vi antigens isolated from ne typhoid strains and the ballerup organism were qual in immunizing potency. There was some suggesion that Vi antigens prepared from *E. coli* may be mmunologically different from the Vi antigens prepared rom the typhoid and ballerup bacilli. *H. J. Bensted*

LARSON, C. L., RIBI, E., MILNER, K. C. & LIEBERMAN, J. E. **A Method for Titrating Endotoxic Activity in the Skin of Rabbits.** *J. Exper. Med.* 1960, Jan. 1, v. 111, No. 1, 1–20, 2 text figs. & 2 figs. on 2 pls. [28 refs.]

The characteristic inflammatory response in rabbits to ntracutaneous injections of culture filtrates or toxic xtracts from Gram-negative bacilli has long been estabished and there has been a good deal of evidence to show hat the intradermal test could be correlated to the lethal est in mice. There has, however, been some argument bout the site of the intradermal injections; the ventral urface of the abdomen is usually chosen for the elicitation f the Shwartzman reaction whereas the site chosen for the ndotoxin titrations is the lateral surfaces of the animal. The authors found that with intradermal inoculations on he rabbit's ventral surface the development of primary esions was too irregular to be of value for titrations, ut when the inoculations were made into the skin of the ateral surfaces visible oedema and erythema usually esulted from doses which were too small to prepare for he Shwartzman phenomenon on any areas of the rabbit kin they tested. Several endotoxins prepared by differnt methods from *Salmonella enteritidis* and typhoid acilli were assayed by this method and the results compared with those obtained with the mouse toxicity test. Statistical analysis revealed excellent correlation etween the mean threshold dose for producing skin esions in rabbits (SLD50) and the median lethal dose or mice (LD50). For potent endotoxins (LD50=0·2–0·3 mgm.) the skin test dose was about one-thousandth f the lethal dose for mice. The method is said to be pplicable to endotoxins from other species of Gramegative intestinal bacilli. *H. J. Bensted*

BILLAUDELLE, H. & LUNDBLAD, G. Studien an *Salmonella typhi*. 1. Physiko-chemische Untersuchungen an mit Hilfe des Frier-Tauverfahrens gewonnen bakteriellen Extrakten. [**Studies on** *Salmonella typhi*. **I. Physico-Chemical Study of Bacterial Extracts produced by the Freezing and Thawing (FT) Method**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Mar., v. 119, No. 3, 295–316, 13 figs. [Numerous refs.]

The methods used in splitting different fractions from he *Salmonella typhi* which are likely to be significant as antigens are described. The main steps adopted in his analysis have been to prepare an aqueous extract of material repeatedly frozen and thawed, and after separating the bacterial stromata from this to fractionate the aqueous extract by ethyl alcohol or acetone precipitation, the supernatant so obtained consists of neucleotides, nucleic acid and amino-acids, sugars and salts. The precipitate is an amino-acid, lipoid, polysaccharide protein complex.

Detailed data with regard to the chemical and physical analysis of these fractions are given and their value as antigens will be discussed in a later paper.

J. W. McLeod

NESTORESCO, N., POPOVICI, Marcella, VLĂDOIANU, I. R. & TUPA, Sanda. Recherches expérimentales concernant les modifications de la *Salmonella typhi, in vivo* sous l'action des bactériophages Vi adaptés. [**Experimental Investigations concerning** *in vivo* **Modifications of** *Salm. typhi* **under the Action of Adapted Vi Bacteriophages**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Dec., v. 18, No. 4, 527–36.

The investigations reported in this paper are concerned with the changes induced by the action of phage when mixtures of phage and broth cultures of *Salmonella typhi* in collodion sacs were introduced into the peritoneal cavities of rabbits. The strains of *Salm. typhi* used were phage-types A and E and the Vi phages were D_1, E_1 and F_2.

Subsequent cultures from the collodion sacs showed that the typhoid bacillus frequently lost Vi antigen and became phage-resistant. Often bio-chemical changes were observed in both Vi-positive and Vi-negative colonies, whether the latter were lysogenic or non-lysogenic; these mainly concerned the fermentation of arabinose. In some cases the ability to ferment arabinose was retained for long periods.

When phage-type A strain was in contact with phage D_1 no change was observed, but when either phage E_1 or F_2 were in contact with the same strain they tended to lose their original specificity for their own type. When however phage E_1 was in contact with its homologous type strain the propagated phage was unmodified [see ANDERSON and FRASER, this *Bulletin*, 1956, v. 31, 323]. *H. J. Bensted*

NICOLESCO, Marcela. Recherches expérimentales sur des vaccins anti-typhiques, préparés avec la souche Ty_2 et un mélange de souches indigènes. [**Experimental Investigations concerning Typhoid Vaccines prepared from the Ty_2 Strain and from a Mixture of Indigenous Strains**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Dec., v. 18, No. 4, 567–74.

The vaccines tested consisted of a pure Ty_2 preparation, a mixture of Ty_2 with 9 recently isolated local strains of different phage types, a mixture of the local strains without Ty_2 and finally one prepared from a laboratory, isolated 2 years previously. All strains were said to be typical typhoid bacilli in all their characters.

The vaccines were phenolized, prepared after the method of KOLLE, but in the active protection test un-phenolized vaccines were also included. As would be expected, the vaccines without phenol, if they had been alcohol-treated [but this is not stated], showed a higher protection rate in this test than the phenolized vaccines, but the difference between the 4 preparations was not marked. On the other hand with the phenolized vaccines the Ty_2 preparation was clearly superior. The passive protection tests and the serological tests appear to have been undertaken with phenolized vaccines only, and in all these tests the Ty_2 and the Ty_2 mixture with local strains proved to be more efficient than the other two preparations. *H. J. Bensted*

HEYMANN, G. & JANDL, G. Experimentelle Untersuchungen zur Wertbemessung von Typhus-Impfstoffen. I. Mitteilung. Die Schutzwirkung von humoralen Antikörpern verschiedener Spezifität bei der weissen Maus. [**Experimental Investigations in the Potency Test of Typhoid Vaccines. 1st Communication. The Protective Effect of Humoral Antibodies of Different Specificity in White Mice**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Mar., v. 119, No. 3, 279–94. [13 refs.]

The authors endeavour to throw more light on the value of the different available typhoid bacterial antigens in the prophylaxis of enteric fever.

In the absence of a suitable experimental animal liable to a disease analogous to typhoid fever, resort was made to determining the capacity of typhoid antigens to stimulate the rabbit to produce antibodies capable of protecting mice from lethal injections of living typhoid bacilli. Protection was found to be best demonstrated if the antiserum was injected 48 hours before the infecting dose of bacteria.

Strains were selected which contained Vi, O-9 and H-d antigens or combinations of these, and by absorption, sera were prepared appropriate to the different antigens. It was clearly demonstrated that sera containing Vi antibodies protected against strains in which Vi antigen was abundant, whereas sera with O-9 antibody only did not.

The converse was not so clearly proved since all sera protected mice from the strain, Ty. 447, which contains Vi, O-9 and H-d antigens and is only moderately pathogenic to mice. Against the highly mouse-pathogenic strain *Salmonella gallinarum* which is well provided with O-9 antigen, serum protection was less effective and there was no significant contrast between antisera rich in Vi antibody and those with a high content of O-9 antibody, as determined by their agglutination titres.

There was no clear evidence for the efficacy of H-d antibody in this type of experiment. *J. W. McLeod*

SCHOLTENS, R. T. **Comparison of the Felix and Callow System of Phage Typing of** *Salmonella paratyphi* **B with the Natural System used in the Netherlands. Results of Members of the First Subcommittee on** *paratyphi* **B of I.C.E.P.T.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25. No. 4, 403–21. [21 refs.]

The title of this paper gives a very good indication its scope. The author brings forward evidence and ar ment to support his claim that the system of pha typing of paratyphoid B used in the Netherlands superior to that of FELIX and CALLOW [this *Bulle* 1943, v. 18, 865; 1951, v. 26, 1116]. It is highly techni and must be read in its entirety; it is not suitable abstraction. *H. J. Benstec*

THOMAS, Constance & WILSON, J. B. **Association Resistance to Bile Salts and Virulence in** *Salm nella typhimurium* **Strains.** *Proc. Soc. Exper. Bi & Med.* 1960, Feb., v. 103, No. 2, 292–4, 1 fig.

A strain of *Salmonella typhi-murium* which could r be cultivated in media containing high concentrations bile salts was found to be less virulent for mice than mutant strains which were not inhibited under the sa conditions. The strain, whose growth was inhibited the presence of bile salts, was found to be truly sensit to the action of these substances, for when this strain w inoculated into liquid bile medium there was relative l of motility quite quickly followed by disintegration the bacterial cells to a significant degree. Although incidence of fatal infections produced by bacteria r inhibited by bile salts was only somewhat greater th those sensitive to their action, they caused much grea tissue damage and were able to persist for longer perio in the host animal. Limited studies with *Salm. pa typhi B* suggest that similar results are likely to obtained with this organism. *H. J. Benstec*

FURNESS, G. & AXELROD, A. E. **The Natural Res tance to** *Salmonella typhimurium* **of the Norm Mouse, Rat and Pyridoxine-Deficient Rat.** *J. I munology.* 1959, Dec., v. 83, No. 6, 627–31, 1 f [29 refs.]

Previous studies by the authors (FURNESS, this *Bu tin*, 1959, v. 34, 1061; FURNESS and AXELROD, *J. Imm nol.*, 1959, v. 83, 133) relating to the effect of cortisc or vitamin deficiency states on rat macrophages influencing infection by *Salmonella typhimurium* in th animals, produced some rather confusing results. In t paper the role of the cellular and humoral defences resistance to infection with *Salm. typhimurium* has be compared in pyridoxine-deficient rats and in normal r and mice. The same strains, used previously, w employed in the present experiments and it was fou that normal rats and mice rapidly clear the majority these virulent bacteria from the blood-stream but tha residual bacteriaemia was always found in the mou The total numbers of the organisms in the liver a spleen of the mouse show a regular tendency to increa this is accomplished by a bacteriaemia, but the numb in the liver and spleen of the rat show a cyclical r and fall, and only when the cycle is at its peak can bacteriaemia be demonstrated. The fall is brought abo by the bactericidal action of the serum on the bacte escaping from the cells of the reticular-endothe

ystem in which the virulent bacterial cells multiply. There was no evidence that pyridoxine deficiency influenced the bactericidal power of the serum or the ability of the cells of the reticular-endothelial system to control the multiplication of the infecting organism.

H. J. Bensted

Nestoresco, N., Popovici, Marcella, Filoti, Aurica & Novac, Stela. Importance de la lysotypie de la *Salmonella typhimurium* comme méthode d'investigation épidemiologique dans les toxi-infections alimentaires. [**The Importance of** *Salm. typhimurium* **Lysotyping as a Method of Epidemiological Investigation in Outbreaks of Food Poisoning**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Dec., v. 18, No. 4, 537–41, 1 diagram.

This is a report on the phage typing of 318 strains of *Salmonella typhi-murium*, 208 of which were isolated from a total of 9 outbreaks and the remainder were presumed to have originated from sporadic incidents. The phage-typing scheme of Felix and Callow [this *Bulletin*, 1943, v. 18, 865; 1951, v. 26, 1116] was employed, but as the work reported here was done before Miss Callow's revised scheme was published it is probable that the number of untypable strains found would have been fewer had the extended range of phages been available. The typing phages employed were sent to the authors in 1957 from the International Reference Laboratory at Colindale and were used over a period of 18 months during which time the reactions remained constant although very slight differences in the intensity of the lytic reactions were noted. The phage-types of the strains isolated from the so-called sporadic incidents were, in the order of frequence:—1a; 2b; 1b; 1; 2; 1a var. 1 and 2a. Types 2d; 3 and 3a were not identified among the strains examined [it will be noted that these type identifications refer to the old designation—see Callow *ibid.*, 1960, v. 35, 300].

H. J. Bensted

Zinder, N. D. **Hybrids of** *Escherichia* **and** *Salmonella*. **The Genetic Homologies of these Bacteria are determined by Mating and Transduction.** *Science.* 1960, Mar. 18, v. 131, 813–15, 1 fig.

Salmonella typhi-murium and *Escherichia coli* are sufficiently different in their characters to warrant their separate generic designation. Nevertheless the gene orders in these two organisms are sufficiently similar to allow genetic recombination to occur. It would seem that the gross features of the salmonella chromosome are the same as those of the coli chromosome; in the same place and in the same order in salmonella and coli we find genes affecting the receptors for a bacteriophage (T6), resistance to sodium azide, fermentation of lactose and arabinose, and synthesis of leucine. In both species the genes for galactose fermentation and tryptophan synthesis lie in other areas. Certain individual differences relative to the interspecific transduction efficiency of different genes may, however, exist.

H. J. Bensted

Guinée, P. & Clarenburg, A. **A New** *Salmonella* **Type** (*S. leeuwarden*). *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 2, 224.

The English summary appended to the paper is as follows:—

"A new *Salmonella* type *Salmonella leeuwarden*, isolated from the stool of a baby, is described.

"The antigenic formula is 11 : b : 1,5."

Dixon, J. M. S. & Wilson, F. N. **Salmonellae in Fertilizers containing Superphosphate.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council)* 1960, May, v. 19, 79–82.

"Salmonella organisms were isolated from mixtures containing infected bone-meal and superphosphate that had been prepared to formulae corresponding to those of proprietary acid-based fertilizers. A neutral phosphate buffer was used for extraction to bring the *p*H of the mixtures to 7·0. Without this neutralization culture was unsuccessful.

"The frequency of isolation of salmonellae from mixtures containing bone-meal and superphosphate was greatly reduced after a period of storage; the organisms were very difficult to detect after dry storage for 6 months.

"There is no reason to believe that compound fertilizers are of importance in the epidemiology of salmonella infection of animals."

Rédey, B. & Csizmazia, F. **The Detection of Unknown Enteric Pathogens by Conjunctival Infection of Guinea Pigs.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 1, 11–18. [13 refs.]

Although Zoeller and Manoussakis (*C. R. Soc. Biol.*, 1924, v. 91, 257) were the first to show that certain dysentery bacilli, inoculated into the eye of a guineapig which had been pretreated with bile, could give rise to an acute inflammatory condition of the conjunctiva, the characteristic guineapig keratoconjunctival reaction to shigella organisms is usually associated with the name of Serény (*Acta Microbiologica*, Budapest, 1955, v. 2, 293), who independently made similar observations and since has much exploited the test [see this *Bulletin*, 1958, v. 33, 690; 1959, v. 34, 567, 673; 1960, v. 35, 191]. The object of the paper under review is to show that the reaction is not confined to accepted members of the shigella group, but that certain of the pathogenic *Escherichia coli* whether or not they are known to cause dysenteric symptoms, may give rise to a purulent keratoconjunctivitis in guineapigs. In other words, in spite of the claim of others for the shigella-specificity of the test it should be regarded as a test for pathogenicity or virulence of the organism under test and that these organisms need not belong to the shigellae. It is well known that many members of the *Escherichia* and the *Shigella* groups share somatic antigens and it is of particular interest to note that one of the authors' *E. coli* types (0 124), which

gave a positive eye test, was identical in its antigenic structure to *Shigella dysenteriae* 3. *H. J. Bensted*

SEN, R. **Cystine as an Essential Amino-Acid for the Growth of a Strain of** *Shigella dysenteriae* **1** (*Sh. shiga*). [Correspondence.] *Nature.* 1960, Jan. 23, v. 185, 267–8.

In studying the nitrogen requirements for the growth of various members of the *Shigella* group in a chemically defined medium with the different nitrogen sources added singly, one strain of Shiga's bacillus was found to be cystine-dependent. That is to say cystine was the only amino-acid among the nitrogen sources which promoted growth of this particular strain. *H. J. Bensted*

VICARI, G., OLITZKI, A. L. & OLITZKI, Zahavah. **The Action of the Thermolabile Toxin of** *Shigella dysenteriae* **on Cells cultivated** *in vitro. Brit. J. Exper. Path.* 1960, Apr., v. 41, No. 2, 179–89, 6 figs. on pl. [18 refs.]

The thermolabile toxin of the Shiga dysentery bacillus exerts a strong cytopathogenic effect on different strains of cells in tissue culture. KB cells, human liver and monkey kidney cells are equally sensitive towards the action of the toxin under optimum conditions, but liver and kidney cell cultures may contain some cells which differ in their sensitivity from the others. The authors found KB cell cultures gave more uniform results. The cytopathogenic effect was specific and the degenerative process, starting with thickening of the cell membrane and ending with a complete destruction of the cytoplasm and pyknosis of the nucleus, was considered to be unlike that seen with any other bacterial toxin. The sensitivity of the test may be judged by the fact that 0·001 mμgm./ml. of culture fluid visibly damaged the culture cells so that the cytopathogenic effect could be used as a sensitive indicator of toxoiding by formaldehyde. The difficulties of completely detoxifying Shiga toxin are well known and it is suggested that this tissue culture method offers a reliable method for the determination of formaldehyde detoxication. *H. J. Bensted*

PENNER, A. & BERNHEIM, Alice I. **Studies in the Pathogenesis of Experimental Dysentery Intoxication. Production of Lesions by Introduction of Toxin into the Cerebral Ventricles.** *J. Exper. Med.* 1960, Feb. 1, v. 111, No. 2, 145–53, 1 fig. [16 refs.]

With dogs as the experimental animals a method was devised for the introduction of Shiga toxin into the third ventricle by inserting a plastic tube through the fourth ventricle into the iter up to the level of the corpora quadrigemina. For the most part, purified Shiga toxin was used in the experiments and it was mixed with a few crystals of trypan blue in order to identify the area in which the toxin was placed for post-mortem check.

In successful experiments there was intense congestion of the anterior pituitary which marked it clearly fr the posterior lobe. The mucosa of the stomach and upper part of the duodenum was also congested petechial haemorrhages often accompanied the cong tion of the stomach. The middle third of the co usually showed a similar picture with, occasionally, gr haemorrhage into the lumen of the gut. The changes the other organs were less regular but there was of congestion of the adrenals at the cortico-medullary ju tion. There was no true pulmonary oedema though larger vessels were well filled.

The toxin was in contact with the parenchyma of central nervous system in a concentration below a le at which an intravenous injection of such a dose wo produce a lesion. If the dose actually employed for intraventricular injection had been given intravenou to the intact animal it would have elicited no respon The observations recorded support the thesis that Sh toxin activates some mechanisms in the central nerv system which are capable of producing visceral lesio *H. J. Benstec*

FORMAL, S. B., NOYES, H. E. & SCHNEIDER, H. **Expe mental** *Shigella* **Infections. III. Sensitivity Normal, Starved and Carbon Tetrachlor Treated Guineapigs to Endotoxin.** *Proc. S Exper. Biol. & Med.* 1960, Feb., v. 103, No. 415–18.

FORMAL and his colleagues [this *Bulletin,* 1959, v. 158, *Bact. Proc.,* 1958, p. 77] have previously shown t fatal infections with *Shigella flexneri* 2a may be produ in guineapigs if they have been starved for 4 days pre ously or given a subcutaneous injection of carbon tet chloride 1 to 2 days before they have been given an o dose of viable organisms. The mechanism of t increased susceptibility is not clear. One toxic prod of the dysentery bacillus is the somatic antigen or endotoxin, and in an attempt to relate the differences susceptibility to *in vivo* distribution of endotoxin, it v decided to repeat the previous experiments with int venous injections of endotoxin in place of the ora administered living organisms. A Boivin-type endoto was prepared from *Sh. flexneri* 2a, the nitrogen conc tration of the final solution was 0·05 mgm. per ml. some experiments endotoxin labelled with ^{51}Cr was u so that the distribution of the endotoxin in the organs the animals could be determined.

The LD50 of the endotoxin used for normal guin pigs was more than 1,300 μgm.; for starved animals was 52·8 μgm. and for animals treated with carbon tet chloride it was 4·2 μgm. The distribution of endoto in the liver and other organs was the same in norm animals and those treated with carbon tetrachloride. T major changes induced by both starvation and carb tetrachloride are to be seen in the liver; starvation gi rise to fatty changes but carbon tetrachloride, in addit to fatty changes, causes a central lobular necro Although this observation would offer a reasona explanation for the decreased resistance of the trea animals if there were obvious differences in the distri tion of endotoxin in the organs, it still seems reasona

o speculate that while the damaged liver could remove he endotoxin from the blood stream it would be in some vay deprived of the power of inactivating it.

H. J. Bensted

MULCZYK, M. Badania nad zmiennością antygenową pałeczek *Shigella flexneri* 1b. **[Studies on the Antigenic Variability of *Shigella flexneri* 1b]** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 1, 1–36. [77 refs.]

The English summary appended to the paper is as ollows:—

"The experiments on the antigenic variability of *S. lexneri* strains were made on experimental animals and rtificial media. It was found that when passaged on vhite mice, *S. flexneri* 1b lose their type antigen I and cquire type antigen III. The composition of group ntigens is not affected. Moreover, it has been demon- trated that the change in the antigenic structure is ccompanied by an alteration in the susceptibility of trains to test phages and that the phage variants of *S. lexneri* subtype change in the same way. It was also hown that the changes acquired by *S. flexneri* during assaging are permanent; the strains maintained for 12 nonths on artificial media behave in the agglutination est and in the presence of phages in the same way as hanged strains, isolated from mice. It was found that he change of antigenic structure of the strains under xamination, accompanied by the alteration of the suscep- ibility to phages, does not affect biochemical properties.

"On passaging the strains on artificial media no trans- ormation of 1b type into the serological variety type 3 ould be observed.

"The experiments with the use of phages showed in he initial cultures of *S. flexneri* 1b (antigenic formula : 3, 4, 6) the presence of mutants with the antigenic ormula III : 3, 4, 6 identical with the changed strains, btained from mice. These mutants occur in intial cul- ures with the frequency of about 1 : 10,000. The initial ultures also revealed the presence of variants with the ntigenic formula identical with the initial culture, as ell as changed susceptibility to phages, corresponding o that of the mutant with the antigenic formula III : 3, , 6.

"Discussing the mechanism of the variability, the uthor explains it by a spontaneous mutation and ssumes that the living organism or bacteriophage is a electing factor.

"Further experiments showed that all changed strains, olated from mice, as well as those recovered *in vitro* ith the use of phage, exhibit an additional antigen, bsent in other *S. flexneri* types and subtypes, namely a ermolabile type antigen. Detailed characteristics of is antigen demonstrate that its physicochemical pro- erties are most similar to those of α^{62}, β^{54}, γ and ^{65} antigens and identical to the thermolabile ϵ anti- en, described by the author [52]. The additional type ntigen of artificially obtained mutants with the antigenic tructure III : 3, 4, 6 is also serologically identical with he antigen ϵ, which occurs in similar strains of this ype, found in natural conditions."

GRZYBEK-HRYNCEWICZ, Kryspina. Zmienność antygenowa pałeczek *Shigella flexneri* 4b. **[Antigenic Variability of *Shigella flexneri* 4b]** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 1, 37–48. [20 refs.]

The English summary appended to the paper is as follows:—

"Subtype 4b, passaged intraperitoneally on white mice was found to lose its type antigen IV and acquire the type antigen III, the composition of group antigens remaining unaffected.

"In addition to antigen III, the serologically changed strain also acquired a new antigen, absent in all standard *S. flexneri* strains. The new antigen was found to be thermolabile and serologically identical with the antigen described in serological varieties of *S. flexneri* 3, occurring in natural conditions or on passaging the subtype 1b on mice.

"On passaging the 4b strain on artificial media, no serological change consisting in loss of type antigen IV and acquisition of antigen III, could be detected; nor did standard and changed strains show any differences in their biochemical properties."

POGONOWSKA-GOLDHAR, J. **Comparative Investigations on Chemical and Antigen Structure of Two Strains of *Sh. flexneri* occurring in Smooth and Rough Forms. I. Chemical Investigations.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 1, 9–13, 1 diagram. [13 refs.] **II. Serological and Chromatographic Investigations.** *Ibid.*, 15–18.

I. Both rough and smooth forms of *Shigella flexneri* have a similar protein-lipid-polysaccharide symplex but the structure is not quite the same. There are no differences in the protein fractions of the two forms, but the differences consist in some shifts within the protein-polysaccharide-lipid ratio. Hydrolysis of the smooth lipopolysaccharide with 5% CH_3COOH gives a phospholipid with a small amount of protein and polysaccharide whereas the lipopolysaccharides of rough strains yield a lipid and a phosphorylated polysaccharide characterized by a sugar content slightly higher than that of the original lipopolysaccharide.

II. Serological investigations showed that all the fractions examined were antigenically active, the lipopolysaccharides and polysaccharides being the most active. There was a considerable amount of cross reaction; anti-S sera cross reacted with the R antigens and *vice versa*, but homologous titres were higher. The chromatographic studies showed that there were differences in the polysaccharide content of the rough and smooth forms. Glucosamine and rhamnose are present in the smooth form, but only as traces in the rough form. No difference between the two forms was found in respect of the amino acid make up, nucleoprotein composition or in the composition of the lipids.

H. J. Bensted

SERÉNY, B. **The Dissociation of *Shigella sonnei* on a Culture Medium containing Desoxycholic Acid.** *Acta Microbiologica. Budapest.* 1960, v. 7, No. 1, 51–6.

This is an extension of the author's previous work [this *Bulletin*, 1960, v. 35, 396, *bis*] on the colonial morphology of *Shigella sonnei* as seen on agar plate cultures. His method of classification of the appearance of the colonies with the culture medium containing desoxycholic acid follows the same system described in his previous article; the new medium however imparts a brownish colour to the colony. When the various colonial forms are tested with type-specific sera it is found that there are in group 1, 3 different forms, all of which are mixtures of Phases I and II organisms, in group 2 one form (rarely encountered) containing Phase I antigen only and 2 forms which are agglutinated by Phase II serum only, and lastly in group 3 the true Rough form. The author considers the desoxycholic acid medium suitable for rapid identification of the Sonne organisms. In his hands it proved to be reliable. *H. J. Bensted*

BROWNING, M. H., BOOT, P. A. & STEVENSON, J. S. **Outbreak of Dysentery caused by *Shigella boydii* 4.** *Brit. Med. J.* 1960, May 14, 1483.

This is an account of a small family outbreak of bacillary dysentery caused by *Shigella boydii* 4. The interest of this report lies in the fact that Boyd dysentery is uncommonly seen in Great Britain and in nearly every case outbreaks of bacillary dysentery due to this group of organisms can be shown to be due to importation of the infection from overseas. In this particular instance there seems to be little doubt that the infection was introduced by a relative of the family, a seaman who had recently returned from a voyage which involved calls at a number of continental ports.

[When Boyd was collecting material for his classical investigations of the mannite-fermenting dysentery bacilli one of his main concerns was that the cultures should come from cases of clinical bacillary dysentery. There was some uncertainty at that time about the position of strain P 274 (now *Sh. boydii* 4). We found this organism on several occasions in the Punjab but none of the patients from whom the strain was isolated, as far as can be remembered, had more than a slight diarrhoea of short duration and the stools were free from blood and mucus, with only a few leucocytes. It seemed doubtful, therefore, whether type P 274 could be regarded as an important cause of bacillary dysentery. Nevertheless this particular strain was not infrequently encountered in India and Pakistan and was included as one of the Boyd types. These personal memories of the original type strain were stimulated by the authors of the present article drawing particular attention to the mild clinical picture of the outbreak they describe and its likeness to the cases seen some 25 years ago. The original source of the present infection is not disclosed but *Sh. boydii* 4 is known to occur in some European countries.] *H. J. Bensted*

YAPHE, W. **Effect of Acid Hydrolyzates of Agar the Growth of *Escherichia coli*.** *Canadian Microbiol.* Ottawa. 1959, Dec., v. 5, No. 6, 589–9 1 fig.

Bacteriological agar preparations contain a number different polysaccharides. Some are sensitive to acid a are readily hydrolysed, resulting in loss of gel streng and an increase in reducing power when agar prepa tions are autoclaved for too long a time. The investig tions reported in this paper indicate that the inhibito effect of acid hydrolysates of agar on the growth *Escherichia coli* was due to 5-hydroxymethyl-2-furalc hyde together with an unidentified heat-labile compone *H. J. Bensted*

HUXLEY, H. E. & ZUBAY, G. **Electron Microscope O servations on the Structure of Microsom Particles from *Escherichia coli*.** *J. Molecular Bi* London. 1960, Apr., v. 2, No. 1, 10–18, 8 pls. [refs.]

FRISCH, D. M., GREGORY, J. & VISSER, D. W. **Effec of 5-Bromodeoxycytidine in *Escherichia coli* a Bacteriophage.** *J. Bacteriology.* 1960, May, v. No. 5, 666–73, 3 figs. [34 refs.]

KOHN, A. **Lysis of Frozen and Thawed Cells of *Esch richia coli* by Lysozyme, and their Conversi into Spheroplasts.** *J. Bacteriology.* 1960, Ma v. 79, No. 5, 697–706, 8 figs. [26 refs.]

NETER, E., ANZAI, H., GORZYNSKI, E. A., NOWOTNY, & WESTPHAL, O. **Effects of Lipoid A Compone of *Escherichia coli* Endotoxin on Dermal R activity of Rabbits to Epinephrine.** *Proc. S Exper. Biol. & Med.* 1960, Apr., v. 103, No. 783–6, 1 fig. [15 refs.]

UMBARGER, H. E., BROWN, Barbara & EYRING, E. **Isoleucine and Valine Metabolism in *Escherich coli*. IX. Utilization of Acetolactate and Ace hydroxybutyrate.** *J. Biol. Chem.* 1960, Ma v. 235, No. 5, 1425–32, 3 figs. [27 refs.]

LEHMAN, I. R. **The Deoxyribonucleases of *Escherich coli*. I. Purification and Properties of a Ph phodiesterase.** *J. Biol. Chem.* 1960, May, v. 2 No. 5, 1479–87, 4 figs. [32 refs.]

KATAGIRI, H. & TOCHIKURA, T. **Microbiological Stud of *Coli-aerogenes* Bacteria. Part X. Vario Factors influencing α-Ketoglutarate-Fermen tion.** *Bull. Agric. Chem. Soc. of Japan.* 19 Mar., v. 24, No. 2, 182–7. [Refs. in footnote **Part XI. Influence of the Amount of Availa Oxygen upon α-Ketoglutarate-Fermentation.** *Ib* 188–96, 1 fig. [Refs. in footnotes.]

HARRISON, A. P., Jr. **The Response of *Bacterium lactis aerogenes* when held at Growth Temperature in the Absence of Nutriment: an Analysis of Survival Curves.** *Proc. Roy. Soc.* Ser. B. 1960, June 14, v. 152, No. 948, 418–28, 6 figs.

DIMITRIU, Ofelia, CERBU, A. & VASILESCO, T. La sensibilité de quelques souches de *Brucella* à l'égard du phage anti-*Brucella*. [**Sensitivity of Certain Strains of *Brucella* to Anti-*Brucella* Phage**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Sept., v. 18, No. 3, 475–80, 2 figs. [11 refs.]

The authors obtained from the Gamaleia Institute in Moscow the *Brucella abortus* phage 'Tbilisi' together with phage-sensitive indicator strains and then proceeded to examine strains of *Br. abortus, Br. melitensis* and *Br. suis* in their own collection which totalled 57. There were 26 strains of *Br. abortus* and all were sensitive to the Tbilisi phage, 7 out of 9 strains of *Br. melitensis* were also sensitive, whereas 19 of the 22 strains of *Br. suis* were phage-resistant. *H. J. Bensted*

SCHEIBEL, I. & ASSANDRI, J. *In vitro* **Investigation into the Sensitivity of Different Strains of *Cl. tetani* to Antibiotics.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 4, 435–44, 1 fig. [20 refs.]

These experiments were done at the State Serum Institute, Copenhagen, with 13 strains of *Clostridium tetani*. Tubes of peptone broth also containing 0·5 haemoglobin, 0·25% agar and 0·3% thioglycollate and different concentrations of antibiotic were inoculated either with vegetative cells (2×10^6/ml.) or a suspension of spores (2×10^5/ml.), and observed for growth after 2 and 7 days. Streptomycin was ineffective. Penicillin inhibited the growth of vegetative cells for 2 days usually in a concentration of 0·1 unit/ml. but after 7 days 3 strains were still inhibited by 1, 7 by 10 and 3 not by 10 units/ml. Results with a spore inoculum were similar, though not identical. Some observations were also made on the numbers of survivors in different concentrations. "Persisters" in both low and high concentrations retained their toxigenicity, and it is briefly mentioned that L-forms appearing later than the 7th day were also toxigenic. Oxytetracycline was usually inhibitory at 1 μgm./ml. for 2 days, but only at 10 μgm./ml. after 7 days.

The authors mention that 3 cases of fatal tetanus have occurred in Denmark in injured persons treated only with antibiotics (2 with penicillin and 1 with streptomycin!). For this reason and on the basis of their own findings they issue a warning against relying on antibiotics for the prevention of tetanus. [Few would disagree with this attitude, but these findings must be contested on the ground that the medium was unsuitable. –SH compounds inactivate penicillin; the thioglycollate content therefore fully explains the late growth observed in high concentrations.] *L. P. Garrod*

BONVENTRE, P. F. & KEMPE, L. L. **Physiology of Toxin Production by *Clostridium botulinum* Types A and B. II. Effect of Carbohydrate Source on Growth, Autolysis, and Toxin Production.** *Applied Microbiol.* Baltimore. 1959, Nov., v. 7, No. 6, 372–4, 2 figs. **III. Effect of pH and Temperature during Incubation on Growth, Autolysis, and Toxin Production.** *Ibid.*, 374–7, 4 figs.

II. In a medium of tryptic casein digest and yeast extract, glucose is necessary for maximal growth, for complete autolysis and for highest toxin production. The increase in toxin production is greater than would be accounted for by the increased growth. Maltose was nearly as good as glucose but other carbohydrate sources tested were less so.

III. Observations on the influence of *p*H and temperature on growth, autolysis and toxin production in the same medium showed optimal growth between *p*H 5·5–7·0, and diminished growth between *p*H 7·0–8·3. Toxin production was maximal between *p*H 5·5 and 8·0 but its stability was greater at *p*H 5·5–6·5 while autolysis was maximal in a narrower range 6·5–7·0. There was no toxin production below 10°C. or at 48°C., but at 10–18°C., a temperature at which food is often handled, there is slow accumulation of toxin since it is stable at these temperatures and an incubation of 8 days at such temperature might yield foods containing 5000 MLD/ml. *J. W. McLeod*

ORLANS, Eva S., RICHARDS, C. B. & JONES, Valerie E. *Clostridium welchii* **Epsilon-Toxin and Antitoxin.** *Immunology.* Oxford. 1960, Jan., v. 3, No. 1, 28–44, 12 figs. [34 refs.]

A study of epsilon toxin of *Cl. welchii* type D (ovine enterotoxaemia) has been made. The method of purification of the crude toxin was fractionation on a column of diethyl aminoethyl cellulose powder, with solutions of potassium dihydrogen phosphate as eluants in the range 0·01 to 0·1 molar. The first fraction, *i.e.* that with the more dilute eluant, yielded toxin of a high level of purity, whereas the secondary antigens which could be recognized in gel diffusion plates on the Ouchterlony model when crude toxin was diffusing to antiserum were found mainly in the later fractions. The relatively pure first fractions obtained still contain some non-protein nitrogen, but observations by ultracentrifugalization and immune electrophoresis suggested a product of a high level of purity. The molecular weight was reckoned to be about 38,000, and the level of toxicity was 100,000 MLD/ml. The relatively pure preparation of toxin so obtained did, however, contain some protoxin since the lethal activity was increased by tryptic digestion. Apart from this the methods of analysis did not permit of differentiation between toxin and protoxin.

J. W. McLeod

MARX, A. Contribution à l'étude du métabolisme des amino-acides dans la toxinogénèse du bacille *Clostridium histolyticum*. [**Study of Amino-Acid Metabolism in Toxin Production by *Cl. histolyticum***] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Mar., v. 19, No. 1, 133–6. [13 refs.]

BAIRD-PARKER, A. C. **The Classification of Fusobacteria from the Human Mouth.** *J. General Microbiol.* 1960, Apr., v. 22, No. 2, 458–69, 6 figs. on pl. [Numerous refs.]

FUCHS, G. H. P. & WALTHER, H. J. Beiträge zur Leptospirenzüchtung. II. Mitteilung. Einfluss von Haemoglobin auf das Wachstum pathogener Leptospiren (Zugleich eine Betrachtung zum Anlegen von Blutkulturen). [**Contribution to the Cultivation of Leptospira. 2nd Communication: The Influence of Haemoglobin on the Growth of Pathogenic Leptospirae**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 570–81, 1 fig. [17 refs.]

The English summary appended to the paper is as follows:—

"The influence of hemoglobin on the multiplication and viability of pathogenic leptospirae was tested using Korthoff medium, containing 20 per cent. sheep serum. Eight different Leptospira strains were cultured in media containing increasing concentrations of hemoglobin. Concentrations of 6·75 to 27·0 mg. per 100 ml. medium proved to provide optimal cultural conditions. With respect to the possibility isolating leptospirae from blood samples the addition of 1 to (4) drops of blood to 10 ml. of nutrient medium is recommended."

FUCHS, G. H. P. Die Beurteilung der Leptospiren-Dichte mit Hilfe elektrophotometrischer Trübungsmessungen. Ein Vorschlag zur objektiven Wertbemessung leptospirenhaltiger Nährsubstrate bei Wachstumsversuchen. [**The Estimation of the Number of Leptospirae by Electrophotometric Turbidity Assay**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 2, 239–54, 1 fig. [14 refs.]

The English summary appended to the paper is follows:—

"The advantages of an electro-photometric assay f the estimation of the number of leptospirae present cultures are reported. Zeiss Elko II electro-photome with turbidimetric set was used. Comparison with c counts lead to the determination of the specific correcti factor $4{\cdot}12 \times 10^8$ (lept./ml.). Thus the cell count c be easily estimated. Since this method is independe from personal factors it is superior to all visual bacter scopic methods of density estimation."

MCBRIDE, Mollie E. & GIRARD, K. F. **A Selecti Method for the Isolation of** *Listeria monocyt genes* **from Mixed Bacterial Populations.** *J. La & Clin. Med.* 1960, Jan., v. 55, No. 1, 153–7, 1 f

The method recommended for the isolation of *Liste monocytogenes* is for the original material to be inoc lated into tryptose phosphate broth (Difco), rehydrat and autoclaved at 15 lb. pressure for 15 minutes w added Furacin 1:10,000 to make a final concentrati of 1:100,000. Sub-inoculation on to the selective so medium is then made. This consists of: Phenyl ethan agar base (Difco) containing trytose 1%, Bac extract 0.3%, NaCl 0·5%, Bacto agar 1·5% and phen ethanol 0·25%. To this is added lithium chloride 0·05 glycine 1% and blood 5%. On this medium *L. mon cytogenes* forms characteristic grey colonies, with zone of haemolysis, which can be readily distinguish from the colonial forms of staphylococci, streptococ *Escherichia, Pseudomonas, Proteus* and *Bacillus subti* and from artificially mixed cultures of these organis *L. monocytogenes* has been isolated without difficul The method has not, however, been extensively tried o with natural clinical material and further work may see desirable in view of certain difficulties which may encountered. *H. J. Benstead*

BACTERIOPHAGES

CETIN, E. T. **Heat Labile and Heat Stable Factors and Antibodies in Normal and Immune Sera against T-System Bacteriophages.** *J. Hygiene.* 1960, Mar., v. 58, No. 1, 35–43, 6 figs.

Serum from normal guineapigs and rabbits inactivates phages of the T system, and it was found that although heating the sera at 58°C. for 60 minutes reduced the amount of phage-inactivating factor, some still remained. Guineapigs were immunized with T2, T3 and T4 phages and the development of neutralizing antibody followed. Antisera were also shown to contain heat-labile and heat-stable activity. Neutralization curves drawn by plotting log percentage of phage survivors against time were concave for fresh sera and straight lines for heated se There was evidently less of the heat-labile factor in bo normal and immune sera. On dilution, curves f unheated sera became straight lines and the heat-labi factor decreased more quickly than the heat-stable or In experiments in which more phage was added to t phage-serum mixture, it was found that the heat-labi was exhausted before the heat-stable antibody.

Complement had no effect on the inactivation of T T3 and T4 by either normal or immune guineapig seru This was shown by adding to mixtures of phage a heated serum fresh normal guineapig serum which h been absorbed in the cold so that phage antibody h been removed without altering the level of haemolyt complement. *Janice Taverne*

HOFSCHNEIDER, P. H. **T_i and λ Phage Adsorption on Protoplast-Like Bodies of *Escherichia coli*.** [Correspondence.] *Nature*. 1960, May 14, v. 186, 568–9, 1 fig.

The adsorption of phages T2, T5 and λ to various strains of *Escherichia coli* was measured after the cells had been transformed into spherical 'protoplast' forms by lysozyme, penicillin, phage enzyme, glycine, or by deprivation of diaminopimelic acid. Phage particles adsorbed at the same rate as with normal bacteria, indicating that cell wall phage receptors were still present. The author argues that the spherical forms cannot therefore be true protoplasts since these are by definition bacteria completely depleted of cell walls. He prefers the term 'spheroplast' proposed by BRENNER *et al.* [this *Bulletin*, 1958, v. 33, 972].

[See also DÉNES and POLGÁR, *Ibid.*, 1959, v. 34, 683.]

Janice Taverne

KÁNTOCH, M. Ciepłochwiejna odmiana faga T2. [**Thermolabile Variety of T2 Phage**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 1, 111–15. [13 refs.]

The English summary appended to the paper is as follows:—

"A new phage strain $T2_{tl}$ with increased susceptibility to high temperatures was obtained during the long-lasting maintainance in the refrigerator of T2 phage, active against *E. coli* B.

"Thermolability of this strain was several times higher as compared with standard strain.

"When passaged on susceptible bacteria, the strain was found to keep its enhanced thermolability."

KIHO, Y. & WATANABE, I. **Multiplicity Reactivation of Heat-Disrupted T2 Phage.** [Correspondence.] *J. Molecular Biol.* London. 1960, Apr., v. 2, No. 1, 78–80, 2 figs. [11 refs.]

LANNI, Yvonne T. **Invasion by Bacteriophage T5. I. Some Basic Kinetic Features.** *Virology*. New York. 1960, Apr., v. 10, No. 4, 501–13, 3 figs. [13 refs.] **II. Dissociation of Calcium-Independent and Calcium-Dependent Processes.** *Ibid.*, 514–29, 4 figs. [16 refs.]

I. Compared with T2, the transfer of DNA from phage T5 to *Escherichia coli* F is slow [this *Bulletin*, 1955, v. 30, 257], and, until the process is complete, subjecting the mixture of phage and bacteria to the action of a Waring blendor interrupts infection and prevents the production of new phage. The author has called the transition to the stage at which blending no longer stops infection "stabilization." This paper is an introductory study of some factors which influence stabilization.

For example, increasing phage multiplicity accelerated stabilization and also shortened the latent period. Aerating the bacterial culture was found not only to increase the rate of adsorption of the phage, but also the rate of stabilization. The rate of stabilization was directly related to the absolute concentration of bacteria, and it was accelerated by diluting the infected culture.

The stabilization of T5 in *E. coli* W thus seems to depend upon the physiological state of the bacteria, and the relation to absolute concentration of the bacteria and the effects of aeration suggest that this in turn may depend upon the oxygen supply.

II. In further experiments the rate of injection of phage DNA, measured by transfer of incorporated ^{32}P, was related to stabilization [see above], which was measured by the production of new phage after subjection to the action of a Waring blendor. It was found that stabilization followed the transfer of DNA, and proceeded at the same rate, but that DNA transfer was independent of the concentration of calcium in the medium while a second calcium-dependent step had to occur before stabilization was complete. In the absence of calcium, a "half-primed" stage of infection could be reached at which phage DNA had been transferred to the bacterium but phage multiplication could still be prevented by the action of the blendor. If calcium was added, stabilization followed immediately.

Janice Taverne

SABLE, H. Z., BAGATELL, F. K., WRIGHT, E. M., SPIZIZEN, J. & EDWARDS, Patricia A. **Growth of *Escherichia coli* and Production of Bacteriophage in Defined Media.** *J. Bacteriology*. 1960, Jan., v. 79, No. 1, 81–9, 1 fig. [21 refs.]

VELAUDAPILLAI, T. **Latent Period, Burst Size and pH Stability of some Phages derived from *S. virchow*.** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 4, 310–14. [10 refs.]

GOL'DFARB, D. M. & BROKER, T. N. **The Antiphage Properties of Certain Antibiotics, Antiseptics, Amino Acids and Anti-Tumour Substances.** *Problems of Virology*. London. 1959, v. 4, No. 1, 101–6. [13 refs.] [Translated from Russian.]

This work was done with a single strain of *Shigella flexneri* and a corresponding phage. Each was added to solutions of different concentrations (varying 10-fold) of the substance to be tested: the phage was titrated after 4 hours' contact and survivors in the culture were enumerated after 1 hour. A variety of substances, 23 in all, were tested: 10 (9 amino acids and sodium borate) had no effect on either phage or bacteria, 6 (including 2 preparations of chlortetracycline) reduced the count of the bacteria only, 4 reduced both to a roughly similar degree, but 3 had a much greater action on phage than bacteria. These were Rivanol, mustine hydrochloride and sarcolysin, the 2 latter being described as "anti-tumour" compounds. Some observations were also made on the action of these 2 on phage at intervals after contact with bacterial cells. Some reasons are given for supposing that testing unknown substances for anti-phage activity may serve as a screening test for anti-tumour activity.

L. P. Garrod

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

CIBA FOUNDATION [WOLSTENHOLME, G. E. W. (O.B.E., M.A., M.B., M.R.C.P.) & O'CONNOR, Cecilia M. (B.Sc.), Editors]. Study Group No. 4. **Virus Virulence and Pathogenicity, in honour of J. Mulder.** pp. viii + 114, 8 figs. on 4 pls. & 3 text figs. 1960. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [12s. 6d.]

A distinguished group of virologists met in London on June 15th, 1959 to discuss virus virulence and pathogenicity and to do honour to Professor J. Mulder of Leiden. The formal papers and lively discussions have now been published. Although from an ecological point of view survival rather than pathogenicity is the primary attribute of a successful virus it is nonetheless their capacity to produce disease that makes viruses suitable objects for study by medical workers. The distinction betwen pathogenicity as a character of a related group of micro-organisms and virulence as the expression of pathogenicity of a stable strain which was made by MILES [see this *Bulletin,* 1956, v. 31, 230] is commended. Virus virulence may be considered at three levels: that of populations, of individual hosts, or of cells. The term "virulence" should perhaps be reserved for viruses damaging intact host, those destroying cells in culture being cytocidal. H. R. MORGAN presented a review of the host-cell factors involved in virus adsorption, replication and the production of cytopathic effects (p. 20–28). His own work, showing the importance of certain nutrients in the replication of psittacosis virus in L cells, is briefly reviewed. In recent years a number of healthy cell cultures carrying cytopathic viruses have been described and it is suggested by A. ISAACS that the production of interferon may explain the stability of such carrier cultures. Since both viruses and host cells are variable it is important to use pure clones of both for critical studies of their interaction but even so difficulties arise since pure clones of viruses do not remain stable for long.

Viruses are notoriously variable and even by the crude tests for measuring virulence at present available it has been clearly shown that this varies also. However, there is still room for argument as to the clinical importance of variations in virulence of the virus since, in fact, the expression of virulence is as much dependent upon the resistance of the host as it is upon the virulence of the infecting virus. Indeed, E. D. KILBOURNE argued that there was little evidence for variations in the virulence of influenza viruses since 1918. All the changes in incidence could be explained by herd susceptibility and variations in individual host resistance. The view that the 1957 Asian influenza virus was as virulent as the 1918 strain was to some extent supported by Mulder's finding that about 20% of deaths during the Netherlands epidemic were probably due to a viral lesion of the terminal respiratory bronchioles and alveoli rather than to secondary bacterial infection. Since there is no 1918 strain of influenza virus it is impossible to decide th issue but, as F. M. BURNET said in summing up the di cussions, it is good for the self respect of microbiologis to think that advances in their science were the prin factor in the different mortality in the 1957 as oppos to the 1918 pandemic.

ISAACS suggested that virus virulence may be related some critical concentration of virus in the tissues mu as has been shown to be the case for the virulence ECHO 9 virus for suckling mice [see EGGERS and SABI this *Bulletin,* 1960, v. 35, 406]. This suggestion was su ported by observations of Professor Mulder and D J. F. Ph. HERS showing that a large dose of avirule virus gave similar pathological lesions as a low dose a virulent virus, and similarly D. A. J. TYRRELL and F. BUCKLAND presented evidence from human volunte experiments, with a variety of respiratory viruses, whi are compatible with the idea that good virus multiplic tion is required to produce symptoms. In this sen virulence may confer an evolutionary advantage on virus by enhancing its opportunities for spread. Ho ever, virulence cannot really be said to be of evolutiona significance. The essential point is that there should sufficient virus produced and plenty of opportunity f it to spread to fresh hosts. The complexity of the facto involved is well illustrated by the discussions of th extensive studies, particularly of FENNER [see *ibid.* 196 v. 35, 199], of the spread of myxomatosis in rabbits. Australia the vector for myxomatosis is the mosquit The mosquitoes become infected by piercing the ski lesions and less virulent virus, which causes chronic sk lesions, is clearly at an advantage compared with mo rapidly lethal virus. However, in England, where th vector is the rabbit flea which is infected from the bloo virulent virus is favoured because it is only when th animal dies relatively quickly that high concentrations virus free of antibody will be present in the blood a will kill the rabbit so that the rabbit flea is forced leave its host.

There was also considerable discussion about livi attenuated vaccines. Tyrrell and Buckland presente evidence from the administration of respiratory virus in man showing that it is impossible to predict what th antibody response will be to an attenuated virus. Som times, for example with ECHO 11, it is very goo whereas for other viruses, for example with the Russia attenuated influenza A virus, the response is very poo Burnet and others pointed out that any medical interfe ence has some risks attached to it and the question always whether these risks are justified by the benefi that are likely to accrue. This problem is posed mo clearly at the present time with regard to living poli vaccines. On the one hand there were speakers lik G. W. A. DICK who thought that because the virus cou spread and was variable there was always some dange whereas on the other hand there were speakers lik WILSON SMITH who believed that although the theoretic

angers existed they were probably less than the benefits kely to be conferred by the vaccine. Altogether this is most interesting book, the value of which is greatly nhanced by recording the stimulating discussions that llowed the formal papers. *A. J. Beale*

OCHENOUR, Alice M. & BARON, S. **Viral Sensitivity of Cell Cultures maintained with Skim Milk Medium.** *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 230–33. [13 refs.]

It has previously been shown [BARON and LOW, *cience,* 1958, v. 128, 89] that cells can be maintained in medium containing skimmed milk instead of serum, nd in the present work the susceptibility to virus infec- ons of cells grown in this medium has been investi- ated. Titrations of types I, II and III poliomyelitis virus, types of ECHO virus, 8 types of Coxsackie, vaccinia, nfluenza, 3 types of adenovirus, herpes and measles irus were carried out in primary monkey or rabbit kid- ey cultures, HeLa or Hep-2 cells maintained in parallel n the usual media and in medium 199 containing 20% kimmed milk. The skimmed milk medium did not give ower titres than the usual media except in the case of he adenoviruses, which gave titres 1 log unit lower, due pparently to an effect on the cells [this *Bulletin,* 1955, . 30, 924]. The results show that the skimmed milk nedium does not contain inhibitors of infectivity and is uitable for use in titrating viruses. *D. J. Bauer*

HERRMANN, E. C., Jr., GABLIKS, Janis, ENGLE, Claire & PERLMAN, P. L. **Agar Diffusion Method for Detection and Bioassay of Antiviral Antibiotics.** *Proc. Soc. Exper. Biol. & Med.* 1960, Mar., v. 103, No. 3, 625–8, 4 figs.

Cultures of chick embryo cells in large dishes are noculated with virus (those mentioned are herpes sim- plex, vaccinia, Newcastle disease and West Nile) and l our later covered with a layer of nutrient agar, on which iscs containing substances to be tested are placed after olidification. After 3–4 days' incubation a further layer f agar containing indonitro-tetrazolium chloride is dded: where the underlying cells are growing this is educed in a few hours to a purple-red formazan. If his colour change is present round a disc it means that irus attack on the cells in the culture has been inhibited. This method permits the screening of a large number of roducts, and can also be used to assay their activity. t is mentioned that the action of isatin-thiosemi- arbazone on vaccinia virus, which has been demon- trated in infected mice [BAUER, this *Bulletin,* 1955, v. 0, 628], can also be demonstrated by this method. *L. P. Garrod*

KUBORINA, L. N. **A Study of a Vaccine against Ornithosis-Psittacosis in Experiments.** *Problems of Virology.* London. 1959, v. 4, No. 3, 26–31. [11 refs.] [Translated from Russian.]

The author reports some preliminary work on the mmunization of animals—mice, monkeys and pigeons— by means of live and killed vaccines. The vaccines were prepared from the brains of mice injected intracerebrally with strains of ornithosis virus. Living preparations were given by routes not producing, or not expected to produce, clinical infection. The virus in the killed vaccines was inactivated by 1 in 1000 formalin or 1 in 10,000 merthiolate. *S. P. Bedson*

AVTSYN, A. P., SEMENOV, B. F. & VITING, A. I. **Lesions in the Organs of White Mice due to Intoxication with Ornithosis Virus.** *Problems of Virology.* London. 1959, v. 4, No. 3, 31–5, 2 figs. [Translated from Russian.]

The authors confirm that ornithosis virus produces a fatal toxaemia in white mice when injected intravenously in sufficient dose. They describe the macroscopic and microscopic changes so produced. *S. P. Bedson*

SEMENOV, B. F. **A Study of the Toxic Properties of Ornithosis-Psittacosis Group Viruses isolated in the U.S.S.R. II. Experimental Characterization of the Toxic Properties.** *Problems of Virology.* London. 1959, v. 4, No. 3, 36–9. [Translated from Russian.]

Working with 3 strains of viruses belonging to the psittacosis-ornithosis group the author shows that the toxicity of yolk sac suspensions of these agents is associated with the virus particles. It was unstable on storage disappearing in 10–14 days at 4°C. and proportionately more rapidly at higher temperatures. With a strain of psittacosis virus it was shown that toxicity was lost after heating for 30 minutes at 56°C.; after treatment with 1 in 100 ether for 30 minutes or 1 in 1000 formalin for 2 hours; and that oxytetracycline and chlortetracycline destroyed it when acting in considerable dose for 2 hours. Parallel titrations of infectivity showed that loss of toxicity was invariably associated with a greater or less loss of infectivity. *S. P. Bedson*

CHERVONSKII, C. I. & POPOVA, A. M. **An Antigen for the Ornithosis-Psittacosis Complement-Fixation Test.** *Problems of Virology.* London. 1959, v. 4, No. 1, 67–70. [11 refs.] [Translated from Russian.]

This antigen consists essentially of an ether extract of heated virus. The virus was grown in the yolk sacs of 7-day chick embryos and suspensions of yolk sacs showing an adequate viral content were heated at 100°C. for 30 minutes and extracted twice with ether at concentrations of 1:10 and 1:3. The ether was removed from the pooled extracts by heating in the 37°C. water bath under partial vacuum and the deposit so obtained was extracted with acetone for 1 hour in the 55°C. water bath. After removal of the acetone the deposit was suspended in buffered saline *p*H 7·1 at the rate of 5·0 ml. per yolk sac and merthiolate added in a final concentration of 1 in 10,000. [The antigen is wrongly described as being specific whereas its heat stability and ether solubility, together with the fact that it fixed complement

with trachoma sera, show that it is the group antigen of the psittacosis-lymphogranuloma group.] *S. P. Bedson*

CARRÈRE, L., MANDIN, J. & POURQUIER, M. Multiplication du virus vaccinal en cultures cellulaires. Étude générale. **[Propagation of Vaccinia Virus in Tissue Culture. General Study]** *Ann. Inst. Pasteur.* 1960, Mar., v. 98, No. 3, 335–43, 1 fig. [43 refs.]

Primary monolayer cultures were used of rabbit kidney chick embryo, human amnion and chorion cells and also cultures of a stock strain KB. The authors found that the mitotic index of infected cultures tended to be lower than that of the controls; and also that as cultures (normal or infected) aged the mitotic index decreased. They also demonstrated a decrease in the mitotic index more or less related to the increase in infectivity of culture supernatants. [The latent period of about 60 hours before a demonstrable increase of infectivity seems inordinately long.] *Colin Kaplan*

POSTLETHWAITE, R. **A Plaque Technique for the Titration of Vaccinia Virus in Chick Embryo Cells and Some Features of Vaccinial Infection in this System.** *Virology.* New York. 1960, Apr., v. 10, No. 4, 466–82, 9 figs. [17 refs.]

This paper describes a method for titrating vaccinia virus in chick embryo cell monolayers. No agar overlay is used and the plaques develop to a recognizable size after 36 hours' incubation. Beyond this time the lack of agar overlay facilitates the formation of secondary plaques. Monolayers with plaques may be stained with carbol-fuchsin and stored for several months. The author states that "the ratio of pock count to plaque count has usually been less than two to one", but no figures are given in support. There is a linear dose-response relationship and adsorption of virus to cells appears to be exponential. [See YOUNGNER, this *Bulletin*, 1956, v. 31, 1044.] *Colin Kaplan*

TAYLOR-ROBINSON, D.; RONDLE, C. J. M. **Chickenpox and Herpes Zoster. II. Ouchterlony Precipitation Studies** [TAYLOR-ROBINSON & RONDLE]. *Brit. J. Exper. Path.* 1959, Dec., v. 40, No. 6, 517–20, 5 figs. on 2 pls. **III. Tissue Culture Studies** [TAYLOR-ROBINSON]. *Ibid.*, 521–32, 6 figs. on 2 pls. [15 refs.]

II. The relationship between zoster and varicella viruses has been further studied [this *Bulletin*, 1960, v. 35, 583] in gel diffusion experiments and in tissue cultures. 21 convalescent-phase zoster sera gave lines of precipitation with zoster vesicle fluid, and in 2 cases 3 lines were also obtained with 11 of 22 acute-phase sera. Convalescent-phase zoster sera gave lines with varicella vesicle fluid which coalesced with those arising with zoster fluid; 21 convalescent-phase varicella sera failed to precipitate with zoster vesicle fluid, but 3 sera gave lines of precipitation when concentrated 5-fold by freeze-drying. Lines were also obtained with 10 convalescent-pha zoster sera and the supernatant fluid from amnion c cultures infected with zoster virus and concentrat 25-fold.

III. In primary explant cultures of human amni and fibroblast cells both viruses formed focal lesions; strains of varicella and 21 strains of zoster virus w isolated in tissue culture from vesicle fluids collected to 4 and 6 days respectively after the appearance of t exanthem. Virus could not usually be found in the c ture fluid, although it was possible to demonstrate t presence of extracellular virus in zoster vesicle fluid.

It was possible to carry out neutralization tests tubes of human amnion cells with zoster vesicle fluid the source of virus, and marked neutralization w observed with the sera of patients with varicella a zoster taken as early as 1–3 days after the appearance the exanthem. Cross-neutralization was also observ in similar tests with varicella vesicle fluid. When try sinized infected amnion cells were used as the source virus, neutralization was not so marked, but a conside able reduction in the size of lesions could be observ under the influence of serum antibody. Neutralizi antibody could be found in the sera of 7 persons w had suffered from varicella from 11 weeks to 40 yea previously. The results of the work as a whole suppo the view that zoster is a clinical manifestation of infe tion with varicella virus. *D. J. Bauer*

CEPLEANU, M. & CAJAL, N. Cercetări asupra transmite herpesului la hamsterul auriu (*Cricetus auratu* **[Investigation on the Transmission of Herpes the Golden Hamster** (*Cricetus auratus*)] *Studii Cercetări Inframicrobiol.* 1959, v. 10, No. 3, 34 55, 4 figs. (3 on 2 pls.) French summary.

In experiments carried out on 51 hamsters (*Cricet auratus*) weighing 100 gm. it was found that this anim is susceptible to infection with herpes virus inject intracerebrally and intranasally. Hamsters infect intracerebrally developed fatal meningoencephalitis af an incubation period of 3 days. Inclusion bodies cou be observed in the neurones. After intranasal inocu tion the animals developed a fatal illness with an incub tion period of 5 days characterized by dyspnoea, sialo hoea, cyanosis and signs of encephalitis. Microscopi investigation of the lungs revealed the presence of int stitial bronchopneumonia. No signs of illness we observed in animals inoculated with the virus by t intraperitoneal, subcutaneous or intramuscular rout *D. J. Bauer*

WHEELER, C. E., with the technical assistance C. M. CANBY. **Further Studies on the Effect Neutralizing Antibody upon the Course of Herp Simplex Infections in Tissue Culture.** *J. I munology.* 1960; Apr., v. 84, No. 4, 394–403, 6 fi [27 refs.]

HeLa cell cultures were infected with 1 of 3 strains herpes virus, then, after time for adsorption, differ

mounts of neutralizing antibody were added to the culure medium and the course of infection was followed oth microscopically and by titrating the virus in the nedium. In some experiments cultures were infected vith varying doses of virus and either none or a lot of ntiserum was added, and in others the dose of virus was onstant and the amount of antiserum varied. It was ound that if the medium did not contain antibody all the ells were destroyed by the 7th day after inoculation, ven with doses as small as 100 plaque-forming units. When the medium contained antibody however, none of he cultures were completely destroyed, whatever the size f the inoculum. Although for the first few days all the ells appeared to be infected, small numbers of uninfected cells always survived and cultures were regenerated rom them. Typically the regenerated cultures became ersistently infected "carrier cultures". They could be ubcultured indefinitely, cells and virus both multiplying, rovided that enough cells were transferred and that nough neutralizing antibody was maintained in the nedium. No evidence was obtained of any sort of lysogenic infection occurring in the carrier cultures, and no ells resistant to virus infection were ever detected. The presence of virus in the cultures was demonstrated either by transferring cell debris to uninfected cultures or by removing antibody from the medium when cytopathic effects of infection would appear and become generalized.

Thus neutralizing antibody does not prevent the cell-to-cell spread of herpes in HeLa cell cultures nor does it eliminate the virus. The author concludes that "these findings make it more understandable that recurrent herpes simplex infections are capable of occurring in man despite the presence of high levels of circulating antibody". *Janice Taverne*

Bayer, M. E. Zur Gestalt des Influenza-Virus. [**The Shape of Influenza-Virus**] Reprinted from *Experientia.* Basle. 1959, v. 15, No. 12, 467, 1 fig.

The English summary appended to the paper is as follows:—

"Influenza-virus particles are generally considered to be of spherical shape after conventional fixation in OsO_4. However, after fixation with $KMnO_4$, the elementary bodies of the influenza-virus (type A Singapur I/57)—adsorbed on the surface of erythrocytes—exhibit hexagonal shape in ultrathin-sections."

Horne, R. W. & Waterson, A. P. **A Helical Structure in Mumps, Newcastle Disease and Sendai Viruses.** [Correspondence.] *J. Molecular Biol.* London. 1960, Apr., v. 2, No. 1, 75–7, 6 pls. [14 refs.]

Eaton, M. D., Scala, A. R. & Rouse, Harriet C. **Viral Growth and Oncolysis in Krebs 2 Cells as affected by Substrate.** *Proc. Soc. Exper. Biol. & Med.* 1960, Apr., v. 103, No. 4, 832–6, 3 figs.

The substitution of lactate for glucose in medium containing glucose and glutamine caused an increase in the formation of cell-associated haemagglutinins by Krebs 2 ascites cells infected with neurotropic and non-neurotropic WS strains and the PR8 strain of influenza virus. The tumour-producing capacity of K2 cells, measured by inoculating mice intraperitoneally and examining for tumours, decreased after their infection. This oncolytic effect was also enhanced in the lactate medium, for there was a reduction in tumour-producing capacity of cells inoculated into mice 4 hours after exposure of the cells to virus, *i.e.* before haemagglutinin production was demonstrated. On the other hand, haemagglutinin production and tumour-producing capacity of NDV were not affected by the changes in substrate mentioned above.

D. Taylor-Robinson

Ado, A. D. & Titova, S. M. **A Study of Experimental Influenza in Dogs.** *Problems of Virology.* London. 1959, v. 4, No. 2, 36–41, 1 fig. [Translated from Russian.]

Dogs inoculated with type A influenza virus by intravenous or respiratory routes developed clinical manifestations including upper respiratory catarrh, pneumonia, fever, leucopenia and disurbances of cardiac and respiratory rhythm. Virus identified as influenza A was frequently isolated from respiratory secretions and urine of inoculated animals. Specific antibody rises were demonstrated in infected animals, which were also shown to be immune to challenge for periods up to about 7 months after infection. *H. G. Pereira*

Blaskovic, D., Borecký, L. & Rathová, V. Pokus o dôkaz cirkulácie vírusu chrípky v medziepidemickom období pomocou vnímavých zvierat. [**An Attempt to prove the Circulation of Influenza Virus in a Pre-Epidemic Period by means of Susceptible Animals**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 6, 376–87. [12 refs.] English summary.

Attempts have been made to detect influenza virus during an inter-epidemic period in 1956–57 by exposing ferrets in public rooms and examining the blood to detect the occurrence of a rise in influenza antibody titre. In a preliminary study of the method 12 ferrets were exposed in a chamber of 2·7 cu.m. capacity in which 10, 100 or 1,000 ID50 of influenza virus in a volume of 1 c.c. was dispersed by aerosol, but no rise in titre of inhibiting antibody could be subsequently detected. 12 ferrets were exposed in public rooms in Bratislava (post office, station and hospital waiting rooms) during the daytime for 5–7 days; 1 month later a 2-fold rise in titre of inhibiting antibody to type A virus was found in 2 and a 4-fold rise in 1 ferret; 5 animals showed a 2 or 4-fold rise in titre of type B antibody. 13 of 21 ferrets subsequently handled by a laboratory worker who experienced an inapparent infection with A-prime virus developed a 4-fold or greater rise in titre of inhibiting antibody. *D. J. Bauer*

LUZYANINA, T. I., SALMINEN, A. L. & SMORODINTSEV, A. A. **Peculiarities of the Interaction of Thermostable Inhibitors from Normal Sera with Type A2 Influenza Viruses of the 1957 Pandemic.** *Acta Virologica.* Prague. 1960, May, v. 4, No. 3, 137–45.

13 strains of influenza A2 (Asian) were studied by haemagglutination-inhibition tests. Some were inhibited to high titre by sera from normal horses, guineapigs, rabbits and rats: these strains were defined as "avid"; other strains were not inhibited and were defined as "non-avid". The inhibitory activity was not destroyed by treatment by heat, zymosan, bentonite, trichloracetic acid, RDE, or influenza viruses. It was destroyed by potassium periodate and by trypsin. It was noted that the behaviour of avid strains with inhibitors resembled that of other viruses in the indicator state; also avid strains eluted less well from red cells than did non-avid strains.

[See also this *Bulletin*, 1959, v. 34, 500, 688, 1189; 1960, v. 35, 89.] *D. A. J. Tyrrell*

HENLE, W. & LIEF, Florence S. **Antigenic Analysis of Influenza Viruses by Complement Fixation. IV. Strain-Specific V Antigens in the Serodiagnosis of Influenza.** *J. Immunology.* 1960, May, v. 84, No. 5, 491–500. [13 refs.]

This paper presents the experience gained from the use of type-specific (S) and strain-specific (V) antigens in complement-fixation tests on human sera collected during the Asian (A2) influenza pandemic and in an earlier outbreak of A1 influenza at a boys' school, New Jersey. During the Asian pandemic, paired sera from 800 patients and throat washings from 119 were examined. A2 virus was isolated in chick embryos from 23 patients but only 17 of these developed anti-A2V. However, sera from the other 6 were taken before the 14th day of illness; not the optimal time for anti-A2V detection. In fact analysis of the A2V antibody titres of 98 patients (5 years old or more) revealed that sera had a significant antibody level in every case only from the 18th day onwards. This considerable time required to develop strain-specific antibody was thought to be a reflection of *de novo* production, compared with the relatively rapid formation of anti-S and heterologous anti-A1V which was probably a "recall" phenomenon. However, although children over 5 years produced antibodies, about 40% below 4 years failed to form anti-S and 50% failed to form anti-A1V presumably owing to previous "inexperience" with the virus. The importance of using the V antigen of the infecting virus to obtain positive results was therefore evident. It is also important when the first serum sample contains a high anti-S level and there is no subsequent rise.

The investigation of the A1 influenza outbreak demonstrated that a strain-specific diagnosis could be made in all cases by the 2nd week, this rapid rise of homologous anti-V probably being a result of previous exposure to closely related strains. *D. Taylor-Robinson*

BRAND, G. & SCHMIDT, B. Der Titerverlauf kompl mentbindender V-, S- und L-Antikörper in Ser influenza-infizierter Meerschweinchen. [**The D velopment of Complement Fixing, V-, S- and Antibodies in the Sera of Influenza infecte Guineapigs**] *Ztschr. f. Immunitätsf. u. Expe Therap.* 1960, Feb., v. 119, No. 2, 175–82, 1 fi [13 refs.]

The author has previously detected differences betwe the soluble L antigen present in the allantoic fluid fertile eggs infected with influenza virus and the solub S antigen present in the membrane [this *Bulletin*, 195 v. 34, 95; *Ztschr. f. Immunitätsf. u. Exper. Therap.*, 195 v. 116, 246], and in the present work a study has bee made of the course of development of L, S and V con plement-fixing antibodies in 12 guineapigs infecte intranasally with the A/Germany/1/1953 strain of infl enza virus. Titrations with the respective antigens we carried out on samples of serum obtained 10, 15, 25 an 45 days after infection, and the results were expressed a the differences between the V and S antibody titres an between the V and L titres. The L and S antibody titre showed significant differences in their behaviour, and th results thus offered further evidence of the serologica difference between the L and S antigens. *D. J. Bauer*

MARINESCU, G., SĂRĂTEANU, D., NASTAC, E., DRĂGĂ NESCU, N. & MUŞAT, B. Studiu asupra rezistenţe la infecţia gripală a soarecilor sugari proveniţi di mame imunizate. [**A Study of the Resistance t Influenza Infection in Suckling Mice Born t Immunized Mice**] *Studii si Cercetări Inframicrobio* 1959, v. 10, No. 3, 315–26. [31 refs.] Frenc summary.

The authors have investigated the susceptibility t influenza infection of the progeny of female mic immunized with influenza virus in the perinatal perio Of 16 infant mice born to 3 mothers which survive intranasal infection with influenza virus carried out 1– days before giving birth, 11 were resistant to intranasa infection with 5 LD50 of virus carried out at the age o 1 week, whereas 11 of 12 control mice died. A simila degree of resistance (13 of 17 survived) was seen in th litters of 4 female mice immunized with influenza vac cine in 2 doses given up to 2 days before birth and days later. The litter of a recently vaccinated femal was allowed to suckle for 12 days and then exchange with the litters of unimmunized females; on challeng carried out 2 weeks later all 16 of the first litter die compared with 5 of 23 in the other litters. The result thus show that antibody can be transferred in the mil when a sufficient degree of immunity has developed i the mother. *D. J. Bauer*

PHILIPSON, L. **Separation on DEAE Cellulose o Components associated with Adenovirus Repro duction.** *Virology.* New York. 1960, Apr., v. 10 No. 4, 459–65, 3 figs. [13 refs.]

Tissue culture fluids from HeLa cells infected wit adenovirus are known to contain group-reactive comple ment-fixing (CF) antigens, haemagglutinating antigens

and a protein component ECE responsible for early cytopathic effect.

Earlier attempts to separate these fractions for closer study [Pereira *et al.*, this *Bulletin*, 1959, v. 34, 831; Rowe *et al.*, *Ibid.*, 293] did not clearly differentiate the CF antigen from the ECE component.

In the present report, chromatographic fractionation on a column of N, N-diethylaminoethyl cellulose (DEAE) was investigated with results similar to those described by Klemperer and Pereira [*Ibid.*, 1960, v. 35, 513].

Dialysed tissue culture fluids of adenovirus type 2 were applied to DEAE columns; stepwise elution with buffered sodium chloride solutions of increasing molarity resulted in almost quantitative recovery of the ECE fraction free from CF antigen and from infectious virus particles. CF activity was recovered quantitatively at higher molarity than the ECE fraction; 15% of the infectious particles appeared in the same fraction. Within the limits of the present methods of elution, however, quantitative recovery of infective virus was not achieved. *Derek Hobson*

Pereira, H. G. **Antigenic Structure of Non-Infectious Adenovirus Materials.** [Correspondence.] *Nature.* 1960, May 14, v. 186, 571–2, 2 figs. [10 refs.]

HeLa cells infected with adenovirus type 5 produce, in addition to virus particles, 3 non-infectious antigens A, B and C. Antigen C is serologically related to B, the protein factor causing early cytopathic changes. The complex nature of B was shown by the fact that trypsin treatment completely abolished its cytopathic activity although almost unaffecting its complement-fixing power. Gel-diffusion precipitation supported by chromatographic studies suggested that antigen B was a complex of a trypsin-sensitive protein (β) with the trypsin-resistant antigen C. Further, after staining the precipitation lines with acridine orange the antigenic component (γ) common to B and C was found to be free of DNA although previous work had shown that antigen C contained DNA. The author speculates that complexes of antigen γ with nucleic acid or nucleoprotein might aggregate to form virus particles whereas complexes of the same antigen with protein might form the DNA-free protein crystals observed by others in nuclei of infected HeLa cells.

D. Taylor-Robinson

Bukrinskaya, A. G. **Cytopathic Effect of Type A2 Influenza Virus in Tissue Cultures of Different Susceptibility.** *Acta Virologica.* Prague. 1960, May, v. 4, No. 3, 146–9. [10 refs.]

"Type A2 influenza virus can be passaged in susceptible tissue (human embryo and monkey kidney) causing a cytopathic effect and the formation of haemagglutinin. In human embryo muscle and lung and human amnion; chick embryo amnion, lungs and muscle; rat embryo lung and HeLa cell cultures the cytopathic effect appears in the first passage only when large doses of virus are used for inoculation (10 or more EID_{50} per cell). In this case no infectious virus is formed, or it is present only in low titres. The haemagglutinins accumulating in the culture fluid are non-infectious. No virus multiplication occurs in the 2nd passage in the tissues mentioned. Adaptation of virus to monkey kidney tissue cultures increases its cytopathogenicity and the formation of haemagglutinins. An A2 virus strain of 1959 did not differ in its culture characteristics from strains isolated in 1957."

Döhner, L. Untersuchungen über das komplementbindende Antigen der interstitiellen plasmazellulären Säuglingspneumonie. [**Investigations on the Antigen obtained from the Interstitial Plasma cell Pneumonia of Infants**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Jan., v. 6, No. 1, 57–63, 2 figs. [12 refs.]

This has been assumed to be a virus antigen. Extracts were prepared from material derived from a case. The antigen was obtained by Vivell's technique (*Deutsche Med. Woch*, 1955, v. 80, 1357), an adaptation of the Casals technique for obtaining virus antigens. After removal of lipoid elements by suitable solvents the antigen is dissolved out slowly in the cold in physiological NaCl solution and finally cleared of insoluble components by centrifugation. This antigen was found to be stable within the *p*H range 4–10 but thermolabile at or above 45°C.

It can be resolved by electrophoresis and also by $(NH_4)_2SO_4$ precipitation into many fractions of which a number are active in fixing complement with appropriate antiserum. The most active fractions move with the globulins in the beta-gamma group. There is therefore no question of a single specific antigen.

J. W. McLeod

Westwood, J. C. N., Appleyard, G., Taylor-Robinson, D. & Zwartouw, H. T. **The Production of High Titre Poliovirus in Concentrated Suspensions of Tissue Culture Cells.** *Brit. J. Exper. Path.* 1960, Apr., v. 41, No. 2, 105–11. [16 refs.]

The authors start from the assumption that the average yield of poliovirus from single cells lies between 100 and 500 infective units [this *Bulletin*, 1959, v. 34, 97; 293] and that this yield cannot be easily increased. If high titre poliovirus preparations are required therefore, it follows that the number of infected cells per unit volume must be increased. This can be achieved by growing cells in monolayer culture and reducing the volume of nutrient fluid, as has been achieved by Churcher *et al.* [*ibid.*, 1959, v. 34, 689], or by growing the cells in suspended culture. This paper describes methods of growing cells in suspension and infecting them with poliovirus so that high titre virus fluids are obtained which will produce a flocculating poliovirus antigen without concentration. 2 limiting factors were investigated: (1) the amount of glucose present in the medium and (2) the concentration of sodium bicarbonate buffer. With cells at a concentration of 10^7 per ml. it was found that even with 8 gm. of glucose per litre all the glucose was utilized

in a 16-hour period. The optimal concentration of glucose and of sodium bicarbonate was found to be 4 gm. of each per litre. This enabled the buffer to control the *p*H within tolerable limits.

With this system it was found that with a virus inoculum of 2 plaque-forming units per cell the greatest virus yield was attained. The yield per cell with 10^7 cells per ml. was usually just under 100 PFU per cell, but the absolute titre per ml. was higher than with lower cell densities which gave higher yields per cell. In these experiments it was found essential to use a single growth cycle and therefore a high multiplicity of infection. The optimal time of harvest was 16 to 24 hours. It was found that at this time peak titres both of infectious virus and of flocculating antigen were obtained. The infectivity titre fell with more prolonged incubation although the flocculating antibody titre remained high. The antisera used for titrating flocculating antigen did not distinguish between the C and D components of poliovirus [see LeBouvier, *Ibid.*, 1960, v. 35, 316]. It has subsequently been discovered that a simple physiological salt solution can be used instead of the complex medium employed in the present work. It is concluded, therefore, that it would be possible to prepare very high titre poliovirus preparations for vaccine production provided that a sufficient quantity of cells is available. It is pointed out that the continuous culture technique for ERK cells developed by Cooper and his colleagues [*Ibid.*, 1959, v. 34, 583] provides the technical solution to this problem. *A. J. Beale*

Gerber, P. & Kirschstein, Ruth. **Biological Properties of Ribonucleic Acid from Virulent and Attenuated Poliovirus.** *J. Exper. Med.* 1960, Apr. 1, v. 111, No. 4, 525–32, 1 text fig. & 6 figs. on 3 pls. [23 refs.]

It has previously been shown [see, for example, Alexander *et al.*, this *Bulletin*, 1959, v. 34, 177] that the ribonucleic acid extracted by the method of Gierer and Schramm (*Ztschr. f. Naturforsch.*, 1956, 11b. 138) from poliovirus is infectious and in suitable cells produces virus of the same type as that yielding the ribonucleic acid. In these studies the Mahoney type 1 virus and 2 variants derived from it, LSa which is virulent for mice by the intraspinal route and LSc which is avirulent in mice both intraspinally and intracerebrally and is also highly attenuated for the monkey, were used. In confirmation of previous studies it was found that the RNA derived from these viruses was infectious, was susceptible to the action of ribonuclease but was not inhibited by specific type 1 gamma globulin antibody. It was found that the RNA derived from the various strains had the same t or temperature character as the donor strain. Thus it was found that the RNA from the Mahoney virus was t+, *i.e.* it grew nearly as well at 40° as at 36°C., whereas the LSc strain was t— and the LSa strain was intermediate. Similarly studies were carried out in mice in which it was found that the pathogenicity for mice of the Mahoney LSa and LSc RNA was similar to that of the intact viruses from which the RNA was derived. It is concluded from these studies that the genetic information is contained in the viral RNA. *A. J. Beale*

Coid, C. R., Tobin, J. O'H. & Beswick, T. S. L. **Sensitivity of Monkeys to Subcutaneous Inoculation of the Brunenders Strain of Type-1 Poliomyelitis Virus.** *J. Path. & Bact.* 1960, Apr., v. No. 2, 325–30.

The authors reasoned that since much larger volun can be inoculated into monkeys subcutaneously th intraneurally, it might be advantageous in testing pol vaccine for safety to use the subcutaneous route. It v found on the contrary that the theoretical advantage not occur. 3 out of 11 animals (all treated with co sone) given 400 TCD50+ in 50 ml. of poliovaccine su cutaneously became infected, whereas 7 out of 15 beca infected when given 3·4 ml. by the combined intraneu and intramuscular routes used for routine safety test of poliovaccine. The explanation almost certainly that antibody production stimulated by the vaccine in bits infection. Thus animals given virus in vaccine su cutaneously produced type 1 neutralizing antibod quicker than animals given virus alone. Similarly anim given virus intramuscularly and intraneurally in 3·4 of vaccine produced much lower (and slower appearin titres of type 1 than animals given virus in 50 ml. vaccine subcutaneously. *A. J. Beale*

French, R. C. & Armstrong, R. E. **Thermal Inactivation of MEF1 Poliovirus.** *Canadian J. Microbiol.* Ottawa. 1960, Apr., v. 6, No. 2, 175–(3 figs. [16 refs.]

This most interesting paper describes a careful stu of the thermal inactivation of the MEF1 strain of type poliovirus. The inactivation of virus proceeds logarit mically till about 98% (the exact percentage varies w temperature) is inactivated and then at a slower log rithmic rate. The half-life of virus is about 23 weeks 4°C., 27 hours at 37°C. and 2½ minutes at 52°C. T energy of activation was calculated from the data p sented to be 26,600 calories per mole from 4° to 47° and 202,000 calories per mole from 47° to 55°C. T lower figure is not too far off that reported for the den turation of calf thymus DNA (Geiduschek and Sturt vant, *Abstracts of papers 136th meeting of the Americ Chemical Society*, September 1959) and the higher figu corresponds to that obtained for proteins. The obser tion of Pohjanpelto [this *Bulletin*, 1959, v. 34, 294] th preincubation at 37°C. with l-cystine retards inactivati at 52°C. was confirmed for the MEF1 strain.

[Le Bouvier *Ibid.*, 1960, v. 35, 405, found that the ac vation energy for the D-C conversion in the range 4 52°C. was 203,000 calories per mole.] *A. J. Beale*

De Somer, P., Prinzie, A., De Maeyer, E. & Lamy, Détermination de la valeur antigénique du vacc antipoliomyélitique. [**The Antigenic Value Poliomyelitis Vaccine**] *Bull. World Health Orgnization.* Geneva. 1960, v. 22, Nos. 3/4, 295–3(5 figs. [18 refs.]

This is a full account of the method of potency test of poliovaccine previously described by De Somer *et*

[this *Bulletin*, 1959, v. 34, 587]. This method depends upon the observation that there is a straight-line relationship between the log dose of vaccine and the $\log_2$ mean serum antibody titre of a group of animals inoculated with 1 dose of vaccine. In this method 2 dilutions are made of a reference vaccine and the unknown and each is inoculated into 30 chicks (Rhode Island Reds) which are bled 5 or 6 days later. All the sera are then titrated and the geometric mean antibody titres plotted against the log concentration of virus. This method enables 2 vaccine preparations, which differ by 3-fold, to be distinguished. It has one great disadvantage in that for every test 120 serum samples have to be titrated against all 3 types of poliovirus. This difficulty can be overcome by a modification of the serum neutralization test so that a 1/8 dilution of serum is tested against 5 log dilutions of virus, or by utilizing a 1/8 dilution tested only against 100 TCD as in the antigen extinction method devised by GARD [*Ibid.*, 586]. These methods are as accurate as the method depending upon serum neutralization titres but the statistical work involved is more elaborate.

A. J. Beale

KUBELKA, V., SOUSEK, O. & ŠRAJBR, E., with the technical assistance of V. VESELÝ, E. ŽÁKOVÁ & Z. BURIÁNOVÁ. Příspěvek ke studiu infekční hepatitidy. [**Contribution to Investigations of Infective Hepatitis**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 6, 388–94, 2 figs. on pl. English summary.

A virus (Motol strain) was isolated from the pooled sera of 2 brothers suffering from infective hepatitis by allantoic passage in chick embryos, which on passage in monkey kidney tissue cultures produced a cytopathic effect in a titre of 10^2. On intraperitoneal injection in mice the culture fluid produced fatal hepatitis in a titre of 10^3–10^4. It was also pathogenic to a lesser extent for guineapigs, ferrets, rabbits and rats, and produced lesions on the chorioallantoic membrane resembling those of herpes. 8 months after the isolation of the virus the sera of the 2 original patients contained antibody with a neutralization index of 225 and 925 respectively. Filtration tests indicated that the size of the virus lay between 100 and 200 mμ. The virus did not produce lesions on the cornea of rabbits or rats, and the animals showed no immunity to subsequent intracerebral challenge with herpes virus. The virus caused haemagglutination of human, guineapig, sheep and chick red cells at 4°C. and haemadsorption could be demonstrated with human red cells in infected tissue cultures.

D. J. Bauer

CHANG, Te-Wen & WEINSTEIN, L. **Characteristics of Growth of Encephalomyocarditis Virus in Cultures of Mouse Muscle.** *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 181–3, 3 figs. [11 refs.]

Fragments of abdominal muscle of adult mice were grown in plasma clots in tubes in a medium consisting of 10% inactivated horse serum, 40% bovine amniotic fluid, 40% Hanks solution and 10% bovine embryo extract with antibiotics and soybean antitrypsin. Good outgrowth was obtained after 6–7 days' incubation in stationary conditions. Addition of encephalomyocarditis virus at this time was followed by the development of a cytopathic effect progressing to complete destruction of the culture after 72 hours. The virus in the culture fluid attained a titre of 4 log units. *D. J. Bauer*

FURUSAWA, E. & CUTTING, W. **Histological Changes in Cells infected with Columbia SK Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Apr., v. 103, No. 4, 851–4, 1 fig.

"The changes produced in Ehrlich ascites tumor cells by Columbia SK virus are described, using various staining technics including fluorescent antibody staining."

[See this *Bulletin*, 1957, v. 32, 1010.]

FAULKNER, P., MARTIN, E. M., SVED, S. & WORK, T. S. **Crystallization of Purified Mouse Encephalomyocarditis Virus Particles.** [Correspondence.] *Nature.* 1960, June 11, v. 186, 908–9, 1 fig.

MAYYASI, S. A., SLOTNICK, V. & BROWN, A. **The Adaptation of Venezuelan Equine Encephalomyelitis Virus to Cell Cultures derived from Monkey Brain.** *J. Infect. Dis.* 1960, Mar.–Apr., v. 106, No. 2, 193–6, 1 fig. [12 refs.]

After 12 passages in embryonated eggs, a strain of virus isolated from a donkey was used in MoB cells, a line derived from rhesus monkey brain (probably from connective tissue). Maximum titres were reached after 48–72 hours. About 20 passages were made with the virus in Maben, Chang's liver and HeLa cell lines: titres estimated by intracerebral mouse-inoculation were usually 6·0–8·5 log and each showed cytopathic effects 72–96 hours after inoculation. Passage did not change these characters. In MoB cells, however, after 5 passages the cytopathic effect came 24 hours earlier than in 1st passage and by the 17th passage the cytopathic effect appeared in 24 hours: the changes also increased in intensity with passage. 17th passage material was given 2 limit-dilution passages then inoculated into eggs. This egg virus was compared with the original egg material and the difference in timing and severity of cytopathic effect confirmed. The 2 passage levels were also compared in L cells and MoB cells: both reached similar high titres in MoB cells—the variant 24 hours earlier. The parent strain multiplied as well in L cells as in MoB but the variant (17th passage) gave titres about 1,000-fold lower in L than MoB and reached its maximum titre 24 hours later in the former. No other differences (pathogenicity for experimental animals or chick embryos, plaques, serology) were found between parent and variant strains. *C. E. Gordon Smith*

NYE, E. R. & LIEN, J. C. **Laboratory Transmission of Semliki Forest Virus by *Aedes togoi* Theo.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, May, v. 54, No. 3, 263–4.

"Mouse to mouse transmission of Semliki Forest virus by *Ae. togoi* was demonstrated experimentally. High virus levels, not less than 10^4 mouse I CLD_{50}, were obtained daily up to the 7th day and also on the 31st day after an infecting feed. Although exact end-points for virus levels were not obtained for the first 4 days, a marked eclipse phase as noted by other workers for SFV in *Ae. aegypti* [WOODALL and BERTRAM, this *Bulletin*, 1960, v. 35, 381; CASALS and BROWN, *ibid.*, 1955, v. 30, 81] was not apparent in this single experiment with *Ae. togoi*.

"Transovarial transmission of SFV was not demonstrated.

"The ability of *Ae. togoi* to maintain high levels of SFV for at least 31 days and transmit it experimentally by bite suggests good potentiality for the transmission of other Group A viruses by this species."

DRĂGĂNESCU, N. Meningo-encefalită inframicrobiană aparţinînd grupului transmis prin artropode. Identificarea agentului patogen si studiul leziunilor nervoase produse la soarecele alb. [**Virus Meningoencephalitis belonging to the Arthropod-Transmitted Group. The Identification of the Pathogenic Agent and a Study of the Lesions Produced in Mice**] *Studii si Cercetări Inframicrobiol.* 1959, v. 10, No. 3, 363–9, 6 figs. on 2 pls. [25 refs.] French summary.

In 1958 a virus pathogenic for mice on intracerebral and subcutaneous injection was isolated from the cerebrospinal fluid of a patient resident in the Dobrudja area of Rumania who was admitted to hospital suffering from a febrile illness with psychic disturbance. In cross-neutralization tests the virus was shown to be related to the tick-borne encephalitis group. Histological examination of the brains of mice infected with the virus revealed the presence of meningeal infiltration, glial proliferation, perivascular infiltration, neuronophagia and satellitosis, particularly in the thalamus and brain stem. Demyelination was not observed. *D. J. Bauer*

SALMINEN, A. **Haemagglutination with Tick-Borne Encephalitis Viruses.** *Acta Virologica.* Prague. 1960, Jan., v. 4, No. 1, 17–24, 2 figs. [17 refs.]

4 strains of tick-borne encephalitis virus (from man, goat and ticks) and 1 of louping ill virus after 2–50 mouse passages were used. Antigens were prepared by acetone-ether extraction of suckling mouse-brain suspensions. Haemagglutinins were prepared from all 5 strains: they gave highest titres (320–1280) at *p*H 6·8 and at 4°C. with chick erythrocytes. The strain in its second mouse passage gave poor agglutination patterns. The antigens were stable for at least 2 months at 4°C. and *p*H 9·0 but unstable at *p*H 7·1 or 6·8. 0·2% formalin or ultra-violet light destroyed the haemagglutinins. No elution of haemagglutinin from cells was detected after hours' incubation at 37°C. Several species of erythrocyte were tried: 1-day-old chick and sheep cells were best; adult chick cells gave irregular results; rabbit cells agglutinated only in a narrow *p*H zone at 4°C.; low titres were demonstrated with human and guineapig cells and none with rat and mouse cells. At 37°C. haemolysis sometimes occurred with high haemagglutinin concentrations. Sheep cells were discarded because they were affected by a non-specific inhibitor not detected by chick cells. The effect of cell concentration was studied at an 0·17% suspension chosen: a 2-fold increase in cell concentration decreased the haemagglutinin titre 3-fold. High titres of non-specific haemagglutinin inhibitor were found in chick, human and monkey sera; horse sera had titres below 10. These inhibitors were stable at 100° for 1 minute and at 56°C. for 30 minutes. No difference was found in the sensitivity of different strains of virus to non-specific inhibitor. 1% bentonite removed inhibitor from most sera but reduced antibody titres 2-fold while 2% bentonite reduced antibody 16-fold. No significant differences were detected between the 5 virus strains by cross-haemagglutinin-inhibition.

C. E. Gordon Smith

ALBRECHT, P. **Study of Tick-Borne Encephalitis Infection in Chick Embryos.** *Acta Virologica.* Prague. 1960, May, v. 4, No. 3, 150–59, 22 figs. on 6 pls. [13 refs.]

9-day-old chick embryos were inoculated by the yolk sac with 10% mouse brain infected with the Hypr strain of tick-borne encephalitis virus. Most of the embryos died in 4–5 days. These and younger embryos were taken for histological section before death and studied after staining with toluidine blue and fluorescent antibody. No fluorescence was seen in embryos 24 hours after infection but virus titres of around 10^{-2} were found in skin, muscle, heart, stomach, liver and brain. 48 hours after infection widespread fluorescence could be seen in striated and cardiac muscle, and scattered in cells of the skin, around the oesophagus and stomach, in groups of neurones in the brain, and in sympathetic ganglia: virus titres were generally higher, highest in muscle, stomach and brain. 72 hours after infection bright fluorescent plaques in hyaline necrotic areas were seen in the diffusely fluorescent striated muscle: most of the neurones in the brain were fluorescent as were the cells in the sympathetic ganglia. Virus titres were still higher, highest in muscle and brain.

96 hours after infection there was pronounced oedema of the skin, green discoloration of the liver and marked friability of the tissues. In addition to the fluorescence in muscle, nervous system and skin, it was also seen in Kupffer cells in the liver, in large mononuclears in the spleen, in haemopoietic nests in the yolk sac, in mesenchymal cells of the lung, liver and elsewhere, in the meso- and meta-nephros and in the thyroid. No fluorescence was seen in the lining of the yolk sac or in the chorio-allantoic membrane. Virus titres of around $10^{-5.5}$ were found in skin and brain, and lower titres ($10^{-3.6}$–$10^{-4.7}$) in hea

stomach and liver. Histology revealed only slight degenerative changes except in striated muscle and in the central nervous system. *C. E. Gordon Smith*

LIBÍKOVÁ, H. & VILCEK, J., with the technical assistance of A. STYKOVÁ. **Assay of the Tick-Borne Encephalitis Virus in HeLa Cells. I. Cytopathic Effect and Metabolic Inhibition.** *Acta Virologica.* Prague. 1960, May, v. 4, No. 3, 165–72, 3 figs. (2 on pl.) [15 refs.]

The Hypr strain of tick-borne encephalitis virus was used: one line after 45 mouse passages, and 1 after 42 mouse passages plus 20 or more passages in HeLa cells. Virus was added to the tubes immediately after the cells. Medium containing 10% horse serum was better than with 20% or 40% serum for production of cytopathic changes. 1·5–3·0 x 10^4 cells were also more sensitive than 6 x 10^4 cells per tube. Cultures with 10% heated serum and 1·5 x 10^4 cells were therefore used and non-specific degeneration did not occur before the 7th day. With the HeLa-adapted virus cytopathic changes first appeared after 48 hours and were complete in 3–4 days. With the mouse-brain virus, however, there was great variation in the final degree of cytopathic change from complete degeneration to degeneration of a few cells only. One passage of the HeLa-adapted line in mice did not affect its ability to cause complete cytopathic effect.

A metabolic inhibition test was designed using 1·5 x 10^4 cells per tube. Good results were obtained only with the HeLa-adapted line of virus. With mouse-adapted virus the titre was 10^{-5}–10^{-6} of that of the same material inoculated intraperitoneally in mice: the HeLa-adapted line gave similar titres by all methods, and after 1 mouse passage this property was retained although the titres were increased about 10^5-fold. *C. E. Gordon Smith*

BENDA, R., DANES, L. & FUCHSOVÁ, M. **The Effect of Cortisone on the Course of Tick-Borne Encephalitis Infection in Cynomolgus Monkeys.** *Acta Virologica.* Prague. 1960, May, v. 4, No. 3, 160–64, 4 figs. [16 refs.]

The B3 strain of tick-borne encephalitis virus isolated from ticks [? passage level] was used. 4 *Macaca cynomolgus* [*M. irus*] were given 6,000 mouse intracerebral LD50 intracerebrally and 6,000 LD50 intraperitoneally; a similar number were given 200 LD50 by both routes. 2 monkeys in each group of 4 received cortisone in 3 doses of 45 mgm.: 1 day before, on the day of inoculation, and 1 day later. In the high dose group, 1 cortisone-treated and 1 control monkey died of encephalitis and the other of each survived although histological evidence of encephalitis was found. All these monkeys had viraemia. In the low dose group, however, cortisone had a marked effect. Both the control monkeys had marked viraemia and survived, developing neutralizing antibody: histological examination of the brain of 1 of them showed only minimal changes. Only 1 of the cortisone-treated monkeys had very slight viraemia and this monkey later died of encephalitis—histological changes in the central nervous system were much less severe than the symptoms suggested. The other cortisone-treated monkey had no detectable viraemia and survived 30 days without developing neutralizing antibody—no histological changes were found in its brain.

The suppression of viraemia by cortisone gives a course after infection resembling the behaviour of sub-lethal doses of virus in *Macaca rhesus* [*M. mulatta*].

C. E. Gordon Smith

DANES, L. & BENDA, R. **Study of the Possibility of preparing a Vaccine against Tick-Borne Encephalitis, using Tissue Culture Methods. I. Propagation of Tick-Borne Encephalitis Virus in Tissue Cultures for Vaccine Preparation.** *Acta Virologica.* Prague. 1960, Jan., v. 4, No. 1, 25–36, 3 figs. [30 refs.]

5 strains of tick-borne encephalitis virus isolated from ticks and after 9–20 mouse passages were used. The virus in the cultures was titrated by intracerebral inoculation of mice. All of them grew equally well in trypsinized monkey and rabbit kidney cells, in HeLa cells, in mouse and chick embryo fibroblasts, and in explants of mouse and chick embryo tissue. In chick embryo and HeLa cell monolayers too many cells led to a rapid *p*H drop and a lower yield of virus. With serum-free media the cells did not multiply and the virus little, but in the presence of serum the cells proliferated and the virus multiplied rapidly. The maximum titre was reached after 48–72 hours and a change of medium led to further virus production. Media without serum but containing albumin were found to give satisfactory titres (5·2–7·5 log). Cultures washed before inoculation gave equally high titres. *C. E. Gordon Smith*

ILYENKO, V. I. **A Contribution to the Methods of Producing a Tissue Culture Formolized Vaccine against Tick-Borne Encephalitis.** *Acta Virologica.* Prague. 1960, Jan., v. 4, No. 1, 37–46, 4 figs.

The Absettarov strain of biphasic meningo-encephalitis (BMEV) virus was used [passage level not stated]. In culture medium without cells and with only dead cells, virus disappeared in 2–6 days while in living cultures virus multiplication occurred giving maximum titres after 3–4 days falling off slowly for 10–20 days then more rapidly. The virus multiplied well in monolayers, suspensions and explants of monkey kidney, human embryo and chick embryo, and in monolayers and suspensions of mouse embryo, and in monolayers of human amnion, cynomolgus heart (CMH) and HeLa cells. Actively proliferating dense cultures gave the best growth and growth was increased by changing the medium. 35 other strains of virus were tried with similar results in chick embryo tissue. No change in BMEV was found after 50 passages in chick embryo tissue. Early serial tissue culture passages had very low titres but titres then increased although always lower than in cultures inoculated with mouse-brain virus. Regular cytopathic changes were not seen in human, chick or mouse fibroblasts. Nor were they found in human or chick embryo fibroblasts

infected with 13 strains of tick-borne encephalitis virus, 21 strains of BMEV and with louping ill. BMEV caused cytopathic changes in a Czechoslovak line of HeLa cells which were neutralized by mouse serum, and could be used to perform diagnostic neutralization tests. In another line of HeLa cells multiplication occurred without cytopathic changes. Chick embryo cells showed no changes and infected cells were shown to survive as long as uninfected: cytopathic changes did not appear even after 20–50 passages in chick embryo cells.

1:500 formalin at 4°C. destroyed some of the antigenicity but 1:1000–1:4000 inactivated the virus without antigenic loss in 14–20 days. The antigenic potency was tested by 3 inoculations of 0·25 ml. on alternate days into mice which were challenged on the 19th day. 11 batches of vaccine gave log protection indices of 2·0–6·5.

C. E. Gordon Smith

LEWKOWITSCH, E. N. & SASSUCHINA, G. D. Gewebekultur-Vaccinen gegen Zeckenencephalitis. **[Tissue Culture Vaccines against Tick-Borne Encephalitis]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 4, 448–53.

The Pan strain of tick-borne encephalitis virus was grown in monolayer cultures of chick embryo tissue; the supernatant fluid was harvested at the time of maximum virus titre and inactivated with formaldehyde. With a concentration of 1:2000 inactivation was complete after 12 hours at 37°C. and after 48 hours at 20°C. Mice vaccinated with the inactivated virus developed neutralizing antibody, and satisfactory titres were attained if the vaccine was adsorbed on aluminium hydroxide.

D. J. Bauer

AOYAMA, Y. **Changes of Cultured Cells infected with Measles Virus.** *Japanese J. Exper. Med.* 1959, Oct., v. 29, No. 5, 535–45, 3 text figs. & 33 figs. on 6 pls. [21 refs.]

The development of inclusion bodies and the changes leading to the formation of giant cells have been studied in cultures of trypsinized human and monkey kidney tissues infected with the Sugiyama strain of measles virus and studied in the living state by time-lapse photography under the phase-contrast microscope, and also by fixation and staining in the usual way. During the first 24 hours after infection nuclear movement ceased, and the movement of the cytoplasmic granules and mitochondria became less active. The cells shrank slightly and margination of chromatin took place. Between 24 and 36 hours some cells shrank and became detached. Eosinophilic inclusions surrounded by an unstained halo appeared in the cytoplasm and later also in the nucleus. Between 36 and 48 hours the cells began to fuse, each fusion taking 30–60 minutes, to form small giant ce containing 5–10 nuclei. These giant cells then fused w each other to form large giant cells with up to 1 nuclei, resembling Warthin-Finkeldy cells. Between and 72 hours the giant cells gradually shrank, and th nuclei became pyknotic, and the cells then beca detached from the glass.

D. J. Baue

ARAKAWA, S., NAGASHIMA, H. & KANEKO, T. **Expe mental Study on Measles Virus. 6th Repo Fundamental Investigation for Practical App cation of Vaccine manufactured by the Mou Fixed Measles Virus.** *Yokohama Med. Bu* 1959, Dec., v. 10, No. 6, 304–17. [14 refs.]

Mouse-adapted measles virus in the centrifuged sup natant of a suspension of infected mouse brain was co pletely inactivated by 0·01% sodium ethylmercurith salicylate or 0·01% formaldehyde after 3 days at 37° The inactivated virus gave a protection index of 2 1 units when injected into mice intraperitoneally, follow by intracerebral challenge 3 weeks later. In a compa son of intradermal, subcutaneous and intravenc methods of vaccination in rabbits a somewhat high protection index was obtained with the subcutaneo route. A rise in titre of measles neutralizing antibo was obtained in 22 volunteers and 20 pregnant wom inoculated with inactivated virus by the intradermal subcutaneous routes.

D. J. Baue

CHARLES, A. **An Electron Microscope Study of M luscum Contagiosum.** *J. Hygiene.* 1960, Mar., 58, No. 1, 45–56, 8 figs. on 5 pls. [26 refs.]

Material from 3 molluscum lesions was embedded methacrylate or Araldite and sections were cut a studied under the electron microscope. The tissue w easily orientated so that the development of the lesi and the developmental stages of molluscum contagiosu virus could be followed from recently infected to t heavily infected areas in which the cells are bags of vi and from which the molluscum bodies and the cornifyi scales are shed. The first changes to be seen in the ce were the formation of clumps of dense particles in t nucleus. The nucleus and nucleolus were often vacu lated but the nucleus was not destroyed and there w no evidence of virus development within it. The vi appeared to be formed from definite foci of fin dispersed cytoplasmic "clouds". Virus particles w later surrounded by a double membrane which app ently fused to make a single capsule.

The development of the virus is discussed in det and compared with that of vaccinia and fowl pox described by MORGAN *et al.* (*J. Exper. Med.*, 1954, v. 1 301).

Janice Taverne

IMMUNITY

ROANTREE, R. J. & RANTZ, L. A. **A Study of the Relationship of the Normal Bactericidal Activity of Human Serum to Bacterial Infection.** *J. Clin. Investigation.* 1960, Jan., v. 39, No. 1, 72–81, 2 figs. [23 refs.]

The object of the investigations recorded here was to letermine whether sera from patients with serum protein ibnormalities or from patients with illnesses associated vith bacterial infections showed any reduction in bacteri-idal activity for Gram-negative bacilli. Sera from 36 iealthy donors and from 43 patients were examined and ›nly 3 sera (patients' sera) showed any major difference n bactericidal activity. 2 of these sera failed to kill ›rganisms isolated from the patients' blood supplying he sera. It is suggested that this failure was due to nterference with the normal bactericidal effect by ntibody.

The heat-labile bactericidal property of the blood ippears to play some part in preventing the invasion of he blood stream by organisms infecting the intestine. The evidence to support this thesis is that shigellae which are very rarely found in the blood stream), iso-ated from the faeces are generally sensitive to the bac-ericidal action of the blood whereas a high proportion of salmonellae isolated from faeces or blood, are resis-ant. Although it is not suggested that this resistance mparts pathogenicity to a bacterial strain the power to nvade the blood stream may be related to its survival and subsequent multiplication with the development of a generalized infection.

The authors found little evidence of changes in the bactericidal potency of the serum, as measured by *in vitro* tests, in patients with a bacteraemia or a disease associated with infection. While it may well be true that the bactericidal system may not be so effective *in vivo* as *in vitro* there are indications that the invasion of the blood stream by an organism from the gut is not due to a change in the bactericidal potency of the serum but to the development of resistant variants. *H. J. Bensted*

ROANTREE, R. J. & PAPPAS, N. C. **The Survival of Strains of Enteric Bacilli in the Blood Stream as related to their Sensitivity to the Bactericidal Effect of Serum.** *J. Clin. Investigation.* 1960, Jan., v. 39, No. 1, 82–8, 2 figs. [12 refs.]

The term "enteric bacilli" employed by the authors included *Escherichia coli, Aerobacter, Klebsiella,* para-colon bacilli, in addition to members of the *Shigella* and *Salmonella* groups. The experiments utilized pairs of strains in which one strain of each pair had been found to be serum-sensitive and the other serum-resistant in the *in vitro* bactericidal test, with normal human and normal rabbit sera. Rabbit serum in this respect is comparable to human serum though somewhat less bactericidal. The pairs chosen could otherwise be distinguished from each other by their differing antibiotic sensitivity. Such pairs were injected intravenously into rabbits and samples of blood withdrawn at varying intervals for the determination of the survivors of sensitive and resistant strains respectively by plate counts on suitable media containing antibiotics. The doses of the 2 strains injected into each rabbit were approximately the same, but after 1 minute there was, in most of the experiments, a marked difference in the counts, the resistant strain outnumbering the sensitive very significantly. This effect was still obvious at 15 minutes, but by the end of 2 hours the clearing of both resistant and sensitive strains from the blood stream was very marked though the resistant strain tended to disappear rather more slowly. Complete clearance might be delayed as long as 48 hours, but generally clearance was rapid and there was no very significant difference between the clearance rates of sensitive and resistant organisms. Where sensitive organisms remained in the blood stream for as long as 48 hours there was no change in their degree of sensitivity in the *in vitro* bactericidal test. The authors' previous observations [above] that spontaneously occurring bacteriaemias of this nature are usually caused by serum-resistant organisms leads them to conclude that although their present experiments suggested that the bactericidal properties of the serum play only a minor role in the clearance of a bacteriaemia, they may have an importance not disclosed by the present investigation. *H. J. Bensted*

MAASSEN, W. Das Properdinsystem. 1. Mitteilung. Eine Modifikation zur Messung von Properdin im Serum. **[A Modified Method for the Determination of Properdin in Serum]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, May, v. 119, No. 5, 405–14, 1 fig. [17 refs.]

The English summary appended to the paper is as follows:—

"A method for the determination of the amount of properdin in human and animal sera is described.

"The properdin contained in the test serum is combined with zymosan at 16°C. in a thermostatic container especially developed for this purpose as described in detail. The C'3 activity of the PZ-complex is determined using a standardized RP-serum.

"The advantage of the method described is to allow also the examination of hemolyzed animal sera. Moreover, it permits the examination of animal sera displaying a certain incompatibility with human RP serum. The third advantage is that the complement of the test serum does not meet the complement of RP serum in an uncontrolled manner. Finally, the PZ complex of the test sample does no longer contain $\alpha_2$globulins inhibiting the inactivation of C'3."

LAURELL, Anna B. & REYN, Alice. **Comparison between Properdin Titers obtained in the Zymosan Assay and in the Bacteriophage-Neutralization Assay. 1. Investigation on Normal Human Sera.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 4, 405–18, 6 figs. [Numerous refs.] **2. Investigation on Pathological Sera.** *Ibid.,* 419–28, 5 figs. [31 refs.]

There are several methods of assaying properdin but the two commonly used in clinical investigation are the zymosan assay of PILLEMER *et al.* [this *Bulletin,* 1956, v. 31, 598] and the bacteriophage-neutralization assay of BARLOW *et al.* [*ibid.,* 1958, v. 33, 992, *bis*]. The first paper (to which reference should be made for the methods, statistical analyses and a good bibliography) compares the results obtained with the two tests in 78 normal sera. No correlation was found between the properdin titres in sera tested by the original zymosan assay and the phage-neutralization assay. By means of a modified zymosan assay, it was possible to determine the properdin values in all the sera showing a titre of <1 unit. When 20 sera were tested both by the original and by the modified zymosan assay method, a positive correlation was found: the titres in the latter were approximately twice as high as those in the former. There was only a tendency towards positive correlation between the titres obtained by the modified zymosan assay and those by the phage-neutralization assay.

The second paper records the results obtained on 23 sera from patients with rheumatoid arthritis and 12 sera from cancer patients. There was correlation between the values obtained by the original zymosan assay and the modified zymosan assay, the values by the latter method being about 4-fold higher than those by the former. By the phage-neutralization assay all the pathological sera fell within the range for normal sera, but whereas the median value of the cancer sera did not differ from that of normal sera, that of the arthritic sera was significantly higher. On comparing the titres in the original zymosan assay with those in the phage-neutralization assay, the cancer sera showed a slight tendency to a positive correlation, but the arthritic sera tended towards a negative correlation. When the modified zymosan assay titres were compared with those in the phage-neutralization assay, the cancer sera showed a significant positive correlation, while the arthritic sera again tended towards a negative correlation. The authors feel that caution is necessary in interpreting the results of these assays: the clinical significance of properdin values is not at present understood and factors other than properdin are likely to be at work. *D. A. Cannon*

VOLKERT, M. **Nonspecific Factors influencing the Fixation of Complement. A Working Hypothesis.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 4, 393–404, 1 fig.

The outcome of a complement-fixation experiment is often perplexing because of unexplained occurrences such as the zone phenomenon. The author postulates non-specific factors which could explain these phenomena: inhibitors and anti-inhibitors, occurring in both the antigen preparations and the immune sera. There are some experimental data but the result is largely hypothesis: the author claims merely to attempt to view the problems of complement fixation from another angle. If the theoretical explanation is reasonable, he points out, there are certain implications: *e.g.* the evaluation and comparison of antigen preparations by testing antigens against such immune and normal sera as are available may select the most specific antigen, but the d ference between it and the others may be due to n specific factors and not to any difference in antige specificity. The hypothesis might even mean that in c tain circumstances it should be possible to enhance antigen by adding non-specific anti-inhibitors.

D. A. Cannon

MÜLLER, F. & KLEIN, P. Fluoreszenz-serologisc Darstellung der Komplementbindung an Virus-An körper-Komplexe in der Gewebekultur. [**Fluor cence in the Demonstration of Complemer Fixation to Virus-Antibody Complexes in Tiss Culture**] *Deut. med. Woch.* 1959, Dec. 4, v. No. 49, 2195–8, 2216. [16 refs.]

The recently developed method [KLEIN and BU HOLDER, this *Bulletin,* 1960, v. 35, 524] of increasing sensitivity of the complement-fixation test, by detect small amounts of complement fixed to an antigen-an body complex by means of fluorescein-labelled anti-co plement antibody has been extended to the detection antibody to ECHO 9 virus. Monkey kidney cell cultu 48 hours after infection with the virus were successiv treated with monkey immune serum treated with verse to inactivate complement and diluted beyond the li of the titre of complement-fixing antibody, guinea complement, and fluorescent antibody to compleme and marked fluorescence was observed in cells wh were showing specific degeneration. No fluorescence v obtained when the guineapig complement was inactiva in various ways; the fluorescence was diminished wh unlabelled anti-complement was added, but remain unaffected where the unlabelled antibody was first p cipitated with guineapig complement. The reacti between labelled anti-complement and fixed complem was thus a true antigen-antibody reaction and the spe ficity of the test was demonstrated in experiments w ECHO 9 virus and immune sera to influenza A a herpes viruses in which negative results were obtain Cross-reaction was observed between ECHO 9 and Mahoney strain of type I poliomyelitis virus when l dilutions of the immune sera were used, but the could be made specific by choosing a suitably h dilution. *D. J. Baue*

HAWKINS, J. D. **Further Evidence for the Du Nature of the Third Component of Complemer** [Correspondence.] *Nature.* 1960, May 7, v. 1 483–4.

GUTHRIE, R. K., RENSHAW, L. & ELLOTT, A. Y. **Inf ence of Cortisone on the C'4 Titer in Guin Pigs.** *Canadian J. Comp. Med.* 1960, Apr., v. No. 4, 122–4. [13 refs.]

"Administration of either egg white antigen to guinea pig results in an increase in the C'4 compon as reported previously. Cortisone injections into guinea pig also result in an increase in the C'4 compo ent in about one-half of the animals tested, with

ange in the remainder. Injection of antigen and cortione together under the conditions described result in a gnificant decrease in the C'4 component of complement. hese results confirm the previous report (6) and give ldditional evidence that the C'4 component of complement is involved in the response of an animal to antigen jection."

öss, B. Papierchromatographische Darstellung von Antigen-Antikörper-Reaktionen. II. Mitteilung: Mikropräzipitationen mit Lipidhaptenen aus Mycobakterien und Organen. [**Demonstration of Antigen-Antibody-Reactions by means of Paper Chromatography. 2nd Communication: Microprecipitation of Lipid Haptens extracted from Mycobacteria and Organs**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 1, 72–85. [109 refs.]

The English summary appended to the paper is as llows:—

"Report is made on the use of chromatographical icroprecipitation in the field of lipid haptens. Instead of ie solvent used so far, ethanol, several other solvents are ıggested, which can be mixed with water: Pyridinium, trahydrofurane, dioxane methylal, methyl-glycol and ethanol. Extracts containing lipid haptens were diluted ith the solvents mentioned above, containing cholesterol ıd lecithin. They were precipitated by dilution with stilled water. The small precipitated particles were lsorbed to greater cholesterol-lecithin particles. The ınditions for the specific reactions are described.

"By means of microprecipitation various haptens could e demonstrated. The fat-phosphatide fractions and the ax fractions (Anderson) always contained haptens. he following strains were tested: H 37 Rv, H 37 Ra, a rain of attenuated virulence, Washington I, Ravenel ıd two further bovine strains. The haptens of the wax raction contains the purified wax (Anderson). Only very ew antibodies or not demonstrable ones are produced by ie lipids of the BCG strain. M. timothee and M. phlei ossibly contain no lipid haptens whatsoever.

"The brains of guinea pigs, cattle, monkeys and umans contain organspecific haptens as well in the fracons which are soluble as in those which are insoluble ı ethyl alcohol."

rehmer, W., Maassen, W. & Stöss, B. Der Einfluss von Prednisolon auf die Sensibilisierung mit hitzegetöteten Tuberkelbakterien. I. Mitteilung: Antikörperbildung und histopathologischer Ablauf beim Meerschweinchen. [**Influence of Prednisolone on Sensitization with Tubercle Bacteria killed by Heat. I. Antibody Production and Histopathology in Guineapigs**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 1, 42–54, 4 figs. [28 refs.]

The English summary appended to the paper is as follows:—

"Intratesticular injections of bacteria killed by heat and suspended in liquid paraffin induce a transient severe, hyperergic reaction, which carries all the symptoms of a generalized tuberculous inflammation—from the serological and pathological point of view. The significance of the paraffin oil as an adjuvant is stressed.

"The titers of the antibodies against old tuberculin, fat phosphatide fractions and waxes were determined by means of microprecipitation. Regularly considerable amounts of antibodies against old tuberculin and the wax fraction were produced, whereas the antibody titers against the fat-lipoid fraction varied considerably.

"Attempts to sensitize guinea pigs by means of an extract free of bacteria of the strain H 37 Rv, according to Choucroun, in paraffin suspensions remained without success. Daily injections of Prednisolone-acetate (2 mg/kg body weight) for eleven weeks showed no definite influence neither in the serological nor in the histopathological reactions.

"The poor cortisone-reactivity of guinea pigs is again stressed."

Linz, R. & Mandelbaum, E. Sur la phagocytose *in vitro* des bactéries par les leucocytes de cobaye. I. Aspects quantitatifs. [*In vitro* **Phagocytosis of Bacteria by Guineapig Leucocytes. I. Quantitative Aspects**] *Ann. Inst. Pasteur.* 1960, Apr., v. 98, No. 4, 524–36, 8 figs.

The English summary appended to the paper is as follows:—

"1. In *in vitro* mixtures of guinea pig leucocytes and *E. coli* K12 or *Staphylococcus albus* Twort at 38°, the leucocytes concentration being constant, the phagocytic index decreases according to the bacterial concentration. The percentage of leucocytes taking part in the phagocytosis also decreases.

"2. If the bacterial concentration remains constant, the phagocytic index and the percentage of leucocytes taking part in the phagocytosis increase when the leucocytes concentration decreases.

"3. The phagocytic index and the percentage of leucocytes taking part in the phagocytosis depend upon the ratio bacteria/leucocytes.

"4. The number of leucocytes containing a great number of bacteria also depends upon this ratio.

"5. Even in mixtures showing an intense phagocytosis and with leucocytes containing a great number of bacteria, a few leucocytes able to phagocyte, but containing no bacteria, usually persist."

Book Reviews

EVANG, Karl [M.D.] **Health Service, Society, and Medicine. Present Day Health Services in their relation to Medical Science and Social Structures. Heath Clark Lectures 1958.** pp. viii + 171. 1960. New York. Toronto. London: Oxford University Press, Amen House, Warwick Square, E.C.4. [21s.]

Dr. Evang is the Director General of the Health Services of Norway and was well known in London when his government was there during the Second World War. He regularly represents his country at the Assemblies of the World Health Organization.

The chapter headings are the same as the titles of his Heath Clark Lectures namely: *Introduction; Main Types of Existing Health Services* (pp. 1–34): *The Role of the Hospital* (pp. 35–65): *The Role of the General Practitioner* (pp. 66–94): *The Role of Drugs* (pp. 95–130): and *The Public Health Service* (pp. 131–167). The first distinguishes between 4 different systems for health services: (1) the "Western European" based on the welfare state idea; (2) the American type based largely on free enterprise; (3) the Soviet Russian type of totalitarian state responsibility and (4) the type gradually forming in the technically undeveloped countries. The author finds it impossible to undertake a comparative evaluation: all produce results and all have shortcomings.

The valuable chapter on hospitals deals with the question of whether or not the hospital should have responsibility not only for curative work but also for preventive and public health work and concludes "prevailing conditions and the service needs which are to be met in more densely populated areas of the Western world are such that it is neither possible nor desirable to establish a full-fledged 'integrated health service' based on a hospital".

The author has had 7 years' experience as a general practitioner and his wife 20. He provides a penetrating chapter on the role of the general practitioner and expresses doubt whether the traditional type of general practitioner can survive much longer unless steps, possibly drastic, are taken to assist him to adjust himself to the new framework of the health services.

The chapter on drugs is most illuminating. It deals with the unfortunate, and sometimes serious, side effects of some of the so-called "wonder drugs"; the steps taken to publicize new drugs with the resulting high costs; the risks of addiction and the present-day substitution of drug taking for a healthy way of life. The steps taken in his own and other Scandinavian countries to limit the drugs paid for from public funds to those named on a list which is constantly revised are described.

The last chapter on *The Public Health Service* is a strong indictment of lay administration of the health services and will be read with pleasure by all medical administrators. His remarks on bureaucratization are forthright and worthy of reproduction: "the growth of paper and desk decisions, promotion based on years of experience instead of on qualifications and qualities, all these must be regarded as malignant tumours in the health services of to-day, not to speak of the belief which always grows in any bureaucracy that proble can be solved by circulars and regulations instead of field work". The public health service should have foremost part in the overall planning of hospitals.

The book is well written by one of long experience many fields, and its scientific value is high.

Allen Daley

MILLER, F. J. W., COURT, S. D. M., WALTON, W. S. KNOX, E. G. **Growing up in Newcastle upon Tyn A Continuing Study of Health and Illness Young Children within their Families.** pp. x + 369, 23 figs. & 9 pls. 1960. New Yo Toronto. London: [Published for the Nuffie Foundation by] Oxford University Press, Am House, Warwick Square, E.C.4. [25s.]

This book is dedicated to the late Sir JAMES SPENC who inspired the survey and launched it. It is a wort recognition of a very great man.

The investigation of "A Thousand Families in Ne castle upon Tyne" was designed to answer the questi "what is the incidence and what types of illnesses occ in infancy and early childhood in Newcastle upon Tyne [For a review of the first volume see this *Bulletin*, 19 v. 30, 190.]

This book continues the story as it unfolded up the time when the children attained their fifth birthd *i.e.* during the years 1947 to 1952. A third volume de ing with their years at school is promised. Clo co-operation in this joint enterprise between the Univ sity Department of Child Health and the City Hea Department is maintained.

The 1,142 children in the original survey were bo between May 1 and June 30, 1947: in the first year died and 4 withdrew: during the next four years 5 di 112 were lost by removal and 3 more withdrew. T smallness of the number who withdrew is a striking te monial to the confidence inspired by the members of t team. The regular and special visits of the health vi tors and doctors continued. Continuity of the staff w regarded as important and throughout the 5 years o 6 doctors and 8 health visitors were engaged in the wo though many family doctors and hospitals made th contributions.

The only similar British investigation is the nati wide one under the auspices of a Joint Committee of t Institute of Child Health of the University of Lond the Society of Medical Officers of Health and the Po lation Investigation Committee [see this *Bulletin*, 19 v. 34, 511] but the Newcastle survey being limited to c city and the field work undertaken by a small numb of people is richer in medical detail and individual fam histories.

The families are still badly housed but, in gene their material circumstances are improving. "The ma need of our society is for improved standards of resp sible family behaviour".

During the 5 years the children had 8,467 signific

nesses; an average of 10 per child, of which 80% were fective and of them 61% were respiratory; accidents counted for half the non-infective episodes. More than lf the children attended at least once the out-patient inic of a hospital and 1 in 5 of the children were admitd to hospital.

There is much interesting information on epidemiology g. that the infectivity of chickenpox is much less than usually assumed. Tuberculosis, whooping cough, accients, behaviour problems and tonsillectomy all receive lequate comment. "Respiratory disease, in some form, almost universal during the early years of life" and, befits its importance the section devoted to it is long id valuable. The opinion is expressed that all children ith pneumonia in the first year of life should be admitd to hospital.

More mothers are going out to work but this is eplored as "a child under 5 needs his mother's undided care".

There is much detailed information in the 113 ppendices.

The conclusions lead to suggestions about how all conerned with the upbringing of children—parents, family octors, hospitals, the preventive health services and the aediatric departments of medical schools—could nprove present procedures.

This is a most valuable and instructive book which ould be essential reading for all concerned with chemes for child welfare.

In a book which is so well written and presented it is rring to find that the word "data" which FOWLER says is plural only" is here regarded as a singular noun.

Allen Daley

KNOWLES, John H. [M.D.] **Respiratory Physiology and its Clinical Application.** 256 pp., 8 figs. 1959. Cambridge: Harvard University Press, Mass., U.S.A. London: Oxford University Press, Amen House, Warwick Square, E.C.4. [$7.50; 42s.]

The recent Ciba symposium on the classification of hronic pulmonary emphysema shows that our understanding of this condition is still far from complete. Clinicians, pathologists and radiologists also disagree bout the diagnosis of certain pneumoconioses and correation is poor between their estimates of the severity of he disease and the actual disability. The testing of ulmonary function should play an important part in efining these conditions.

Unfortunately many of the tests measure more than ne lung function; moreover the methods vary from one ospital to another. As in so many other fields there is lso a strong need for more reliable normal values with egressions on age and body size (and for this purpose tem height appears to be generally more suitable than eight, weight or surface area). Closer control of state f activity and ambient temperature may reduce the naccountable scatter in some tests, leading to greater recision in the delineation of normality.

Lung function testing procedures generally give results which are satisfactorily reproducible in normal persons, r in the presence of isolated defective function. Too often the defect is multiple and the factors are difficult to isolate, *e.g.* compliance cannot be accurately measured in the presence of airway resistance, and alveolar-capillary diffusion is a blanket term which, in addition to specific permeability of the membrane, depends on non-uniformity of ventilation, lung volume (or more strictly total area of membrane) and resistance to transfer of gas in the blood.

Lung function testing is more widely practised in U.S.A. than in England and, although the basic tests frequently originated in European countries, their development into useful clinical tools owes much to American workers, especially those at Philadelphia, Boston and Baltimore. The work under review does not mark as great an advance in this subject as *The Lung* by COMROE and his colleagues, when it was published 5 years ago [this *Bulletin*, 1956, v. 31, 1179]. Nevertheless it presents a sound, readable, up-to-date account of pulmonary function tests (122 pages) and of the application of these to lung disease (88 pages). The scope of the tests is now well known: perhaps the greatest advances in the past few years have been made in the measurement of lung mechanics, or the work required to overcome viscous and elastic resistance to breathing. While these more sophisticated procedures are competently described, one chapter is devoted to the fundamental arterial blood studies and in this methods for blood gas analysis are given in detail with valuable hints on the source of error and limits of accuracy.

The clinical portion begins with COURNAND'S classification of pulmonary insufficiency but emphasizes that defects are seldom single. The complicated subject of pulmonary fibrosis is classified under 5 headings: (1) bronchiolar, (2) interstitial (including alveolar-capillary block), (3) parenchymal, (4) pleural and (5) vascular. The diseases in each group are tabulated together with patho-physiology and simple clinical diagnostic aids.

The remaining 11 chapters give excellent accounts of forms of pulmonary disease, mainly chronic, in which lung function testing is most applicable.

The bibliography consists of 426 well chosen works; these are referred to specifically in the text but unfortunately are not listed alphabetically. There are 14 tables and 8 figures. [A list of standard symbols and abbreviations, gas conversion nomograms and more extensive data on normal persons might have been included with advantage.]

This is a most valuable account of lung function measurement and of its clinical application. It is reasonably priced.

M. L. Thomson

BURNET, F. M. & STANLEY, W. M. [Edited by.] **The Viruses. Biochemical, Biological, and Biophysical Properties. Vol. 1. General Virology.** pp. xvii + 609, illustrated. 1959. New York 3: Academic Press Inc., 111, Fifth Avenue, N.Y. London: 40, Pall Mall, S.W.1. [£5 18s. 0d.]

This book is the first of a series of 3 volumes devoted to the viruses, the third and second of which have appeared and have already been reviewed in this *Bulletin* [1960, v. 35, 526, 527].

Volume I is devoted to a consideration of selected topics of general virology, and consists of 11 chapters, each written by different authors who are acknowledged authorities in their subject. The work is devoted not to a description of individual groups of viruses, but to varied aspects of experimental investigation of animal and plant viruses by the techniques of biochemistry and biophysics. As the editors are careful to point out, tobacco mosaic virus and bacteriophage occupy an inordinately large proportion of the subject matter. This is by no means an indication of a lack of balance, but is rather a reflection of the great amount of experimental investigation which is being devoted at present to those branches of virology in which the most important advances are being made. The individual chapters deal with the structural and biochemical features of the host cell, the physical properties of virus particles, titration methods, inactivation by physical and chemical agents, infective ribonucleic acid, the chemical composition of virus particles, insect viruses, immunological techniques and virus multiplication. The book is intended not for the practical worker but for the academic virologist, for whom it will be an indispensable work of reference.

D. J. Bauer

DUBOS, René. **Mirage of Health. Utopias, Progress and Biological Change.** 221 pp. 1960. London: George Allen & Unwin, Ltd., Ruskin House, 40, Museum Street, W.C.1 [21s.]

The designs for perfecting a population inevitably include measures to alleviate stress and disease. Such precautions would only become superfluous when a state of perfection had been reached. Perfect states of mankind with health of body and mind are described by nostalgic poets as having existed in the past in Gardens of Eden and in Arcadias. Travellers tell of similar habitations existing at the present time in desirable but invariably distant climes, while both altruistic and predatory prophets advertise Utopias of the future. Prescriptions for perfection differ considerably according to prospective inhabitants, but one aspect of reality associated with all of them is a certain remoteness due to time or space.

The development of civilizations has had a profound influence on projected Utopias. Such organizations as the Valhallas, provided for the exclusive use of warrior heroes, have become totally outmoded exc by retrogressive movements engaged in romanticiz violence. The facilities provided for mutual slaugh with miraculous recovery and feasting, enabling the sc of an elect to repeat the performance indefinitely, h lost their appeal to the educated. Even the parac promised to those who have developed notable capaci for appreciation of food, wine and sex, allotted accord to the rules of a particular hierarchy, loses its attract to the more mature when prescribed for indefi repetition.

A less exclusive Elysium designed by philosoph assumes a clearer biological and sociological patt where athletes compete, poets declaim and sages ar interminably against a background of music and danci But even this organization, run presumably with adn able smoothness, presents the static staleness of perfect machine. Life as we know it has provided with the material equipment to select or reject toget with the contrasts from which selection and rejection be practised. To appreciate rewards one must rec nize the contrasting values of punishment and may e require a reminder in some form from time to time in type of life to which, for the present at least, we accustomed.

This is the philosophical background from wh *Mirage of Health* is written. Stress and disease, in many different forms in which they exist, are descri in relation to the adaptations of living individuals those of the populations they make up as part of process of evolution. The author, a distinguished b teriologist, surveys the balanced adjustments by means which life as a dynamic process develops these adap tions in many organisms and in man in particular. wealth of interesting and relevant information, dra from aspects of human history and art as well as fr the physical, biological and psychological sciences, ill trates the significance of stress and disease in the em gence of those qualities of humanity on which we pr ourselves as a species—in addition to the other featu of our evolution. The design of idealistic Utopias become an essential, if somewhat empirical, feature human motivation and behaviour and one which we well to continue. But the author reminds us that, w the development of new forms of civilization and n patterns of adaptation to changing conditions, the pl for combating stress and disease are still as likely to quire attention as in the past. *Gordon Scott MacGregor*

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